INTERDIGITATION AND THE DEVELOPMENT OF THE DENTO-FACIAL COMPLEX

An experimental study in growing *Macaca fascicularis*

Een wetenschappelijke proeve op het gebied van de
Medische Wetenschappen.

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Dedicated to Mieke, Frederik and Ann-Sophie

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Chapter 1

General introduction

1.1 Introduction

Many tissues and structures are involved in the growth of the maxillo-facial complex. The development of different entities as the dentition and the skeleton have to be attuned in order to arrive at a harmonious outcome. Deviations in the attuning may lead to malocclusion and skeletal disharmony. Although the regulation mechanisms involved are far from understood, orthodontists interfere routinely in this system. By their therapeutical approaches they try to provide stimuli to guide the growth of the maxillo-facial complex to the ultimate treatment goal: a stable, well-functioning and aesthetically acceptable dentition and face.

Increase in knowledge of the growth process of the maxillo-facial complex and the regulation mechanisms involved will contribute to the improvement of orthodontic treatment procedures. Maxillo-facial growth is intimately associated with nervous, endocrine and paracrine systems, but also with mechanical stimuli which trigger biochemical events on the cellular level. The interest of orthodontists in the role of these mechanical stimuli is obvious, as the majority of orthodontic appliances depends on them as a tool to evoke the desired biological responses.

Mechanical stimuli probably play an important role, although indirect, in the coordination of mandibular and maxillary growth. On the one hand, skeletal growth provides the space needed for development of the dentition. On the other hand, forces evoked by interdigitation may play a role in the regulation of the development of alveolar bone, surrounding structures, and jaw growth.

It is generally accepted that in humans occlusion and interdigitation is established by means of guided eruption of the teeth through the so-called cone-funnel mechanism, mediated by the typical occlusal anatomy of antagonistic teeth (Schwartz, 1951; Slagsvold, 1971; Van der Linden, 1983). Once occlusion is established, mechanical stimuli will be evoked every time the teeth interdigitate. The impact of these mechanical stimuli on the interaction between jaw growth and development of the dentition has been studied in several animal experiments. However, the conclusions of these experiments are not concurrent, probably due to differences in experimental

design, animals used, and quantification techniques.
In an extensive series of experiments in rats, Petrovic and co-workers (1976, 1977), influenced the growth of the maxillo-facial complex in rats by a variety of interventions, including different orthopaedic devices, sectioning of the lateral pterygoid muscle, tongue reduction, and the administration of growth hormones. Their main conclusion was that interdigitation plays a key role in the coordination of the sagittal growth of the mandible and the maxilla.

Kantomaa and Rönning (1985), also using rats, experimentally restricted maxillary growth by creating synostoses of maxillo-facial sutures, with or without elimination of interdigitation. In both situations they found that inhibition of maxillary growth was accompanied by slowing down of mandibular growth. As the effects appeared to be independent of interdigitation, they concluded, in contrast to Petrovic *et al.*, that interdigitation does not seem to play a role in the coordination of mandibular and maxillary sagittal growth.

Extrapolation of findings derived from studies on rats as discussed above to humans is not well possible due to the large differences between the two species. Most essential in this respect are the marked differences in morphology and physiology of the maxillo-facial complex. Data derived from experiments on non-human primates may yield more relevant information (Van der Linden, 1971; Moffett, 1973; Sirianni, 1985; Watts, 1985). Particularly the growth and development of the maxillo-facial complex of members of the *Cercopithecoidae* superfamily of the *Catarhinae* suborder, to which the *Macaca species* belong, are quite well comparable to that of man (Duterloo, 1970; Sirianni, 1985; Enlow, 1990). So *Macaca spec.* has distinct advantages over the other non-human primates and non-primates in the study of growth of the maxillo-facial complex.

The dentition of *Macaca spec.* has the same number of deciduous and permanent teeth as humans and also the dental morphology, and posterior occlusion and interdigitation are highly comparable to humans, although all dimensions are smaller. Also the development of the dentition, including tooth eruption and the sequence of transition, as well as the skeletal growth in the maxillo-facial complex are highly comparable to humans.

In *Macaca spec.*, the deciduous dentition is complete at about 6 months of age; skeletal growth continues until about 6 years of age. Experimental interference can be performed at any stage of the development of the dentition. The patterns and rates of skeletal growth of the maxillo-facial complex show basic similarities with humans (Duterloo, 1970; Sirianni, 1985; Enlow, 1990).

Despite close resemblance to human morphology, several differences exist. In *Macaca spec.* the transverse dimensions of the tooth bearing parts of the maxilla are larger then those of the mandible. Consequently, the maxillary deciduous and permanent molars show a convergent bucco-palatal inclination. Their crowns are located more palatally than their roots, while in humans the reverse situation exists in the molar region. In *Macaca spec.*, the mandibular molars are buccally inclined, and in humans lingually (Fig. 1-1). The width of the mandibular base in *Macaca spec.* is relatively small in comparison to the maxillary one, in contrast to the situation in humans.

Another marked difference is the development of a facial muzzle in *Macaca spec.* as the anterior jaw growth is far more pronounced than that in humans. Furthermore, non-human primates, as most other mammals, have a separate pre-maxilla of which both halves show ossification at an early post-natal stage (Cotton, 1978). Each halve fuses at the lateral side with the maxillary ossification centres, resulting in a Y-shaped configuration. There are strong indications that in humans initially separate pre-maxillary ossification centres are formed, but fusion with the maxilla already takes place in the fetal period (Ten Cate, 1989). Finally, a sexual dimorphism in the maxillo-facial complex, not present in humans, develops in *Macaca nemestrina* (Sirianni, 1985) after the age of three years, but it seems not to show up in *Macaca mulatta* (McNamara, 1976).

Despite the anatomical and physiological differences mentioned above, *Macaca* monkeys offer a good model for research on maxillo-facial growth, especially for studying the role of occlusion and interdigitation (Van der Linden, 1971; Moffett, 1973; Sirianni, 1985; Watts, 1985).

Elgoyhen *et al.* (1972) observed in normal *Macaca mulatta* differences between mandibular and maxillary growth in sagittal direction, while the occlusion remained relatively constant. They suggested that the steeply

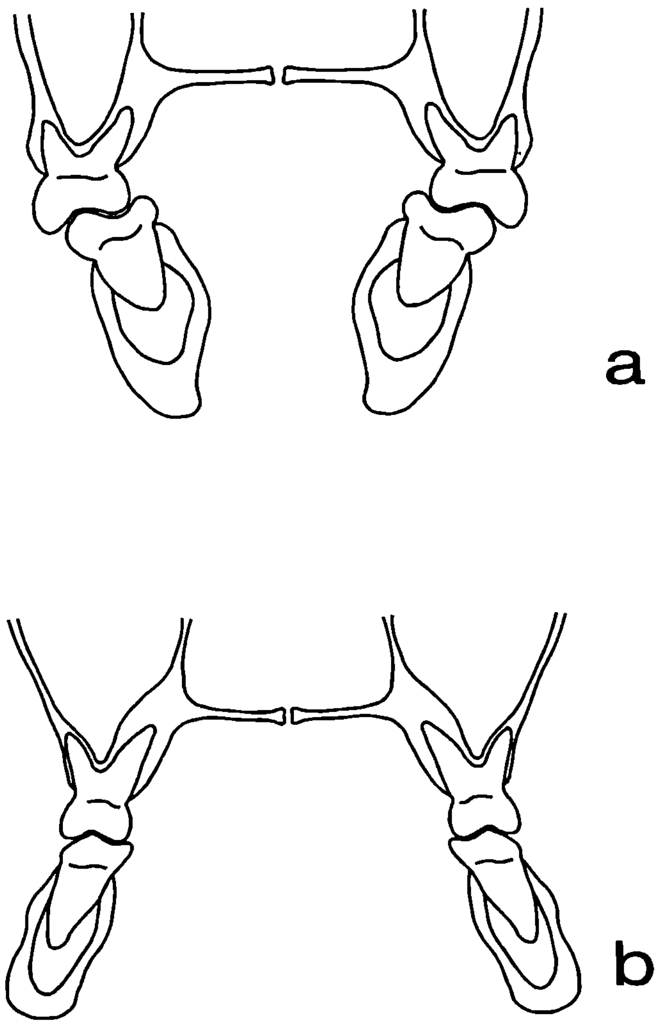

Figure 1-1: *Schematic drawings of a frontal cross-section of the dento-maxillary complex. a: Macaca species; b: man.*

inclined cuspal planes were a contributing factor to occlusal homeostasis The work of Joho (1973) pointed in the same direction He reported that, after application of a distally directed extra-oral force to the mandibular permanent first molars, the maxillary ones moved distally, due to functional transmission of the force applied on the mandible by interdigitation

Sarnat (1976) resected the median and transverse palatine sutures in *Macaca mulatta* and studied the jaw growth thereafter He found that maxillary growth was not significantly influenced by the surgery He concluded that the mandible might guide the growth of the maxilla by means of occlusion and interdigitation

Nanda and co-workers (1983) performed Le Fort-I osteotomies in *Macaca fascicularis* After repositioning the maxilla in a superior position, they found a coordinated reduction in the growth of both jaws, resulting in a normal occlusion They assumed that interdigitation played a coordinating role in mandibular and maxillary growth

Also observations in humans indicated, although on a hypothetical level, a contribution of the interdigitation to skeletal development Lager (1967) emphasized the importance of interdigitation stating that persisting incorrect intercuspation adversely affects the growth of jaws and face Also Slagsvold (1971) and Fishman (1976) emphasized the influence of occlusion and interdigitation on facial development Brace (1977) stated that cusp form in the human dentition is not a prerequisite for effective mastication and he stressed the importance of interdigitation as a guiding system for the developing face Helm (1979), in a study on the prevalence of malocclusion in medieval and modern skulls, reported a marked occlusal and interproximal attrition in the medieval dentition resulting in loss of interdigitation He attributed the concomitant increase of crowding and significant higher prevalence of mesio-occlusion and cross-bites to an unimpeded forward drift of the mandibular dental arch

In clinical orthodontics a contribution of interdigitation to maxillo-facial development is often assumed According to Moyers and Wainwright (1977), the occlusion of the first permanent molars is a determining factor in naso-maxillary and alveolar growth and development Van der Linden (1986) developed a hypothetical model in which a guidance role in the regulation of transverse maxillo-facial growth was assigned to the maxillo-mandibular interdigitation by means of the so-called rail mechanism

In all experimental approaches so far, the original craniofacial development has been disturbed by surgical intervention or by growth restriction or stimulation, which limits extrapolation of these findings to normal growing systems The nonexperimental studies deal, in a hypothetical way with the complex interplay of the development of the dentition at the one hand and the skeletal maxillary and mandibular development on the other hand None of these reports, however, yields conclusive evidence for the way these processes are regulated

To meet this shortcoming, in the present study the contribution of interdigitation to the growth and development of the maxillo-mandibular complex is investigated using an experimental set up in which growth centres are not directly disturbed or affected As experimental animal the *Macaca fascicularis* species was used since its basic plan of growth of face and cranium parallels that found in humans

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Chapter 2

Age assessment in infant crab-eating monkeys (*Macaca fascicularis*) based on tooth development

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2.1 Summary

Tooth development was studied in thirteen *Macaca fascicularis* monkeys with known dates of birth. Regular intra-oral examination was carried out and standardized lateral radiographs were collected under general anaesthesia from 27 until 150 weeks of age.

Three stages of tooth development were determined radiographically: onset of crypt formation, onset of mineralization, and crown completion. A fourth stage, the emergence, was determined clinically. Developmental stages were recorded for six mandibular and five maxillary teeth.

The ages of emergence of the permanent teeth and the developmental stages of the third molars showed the largest variation. A significant sex difference with earlier maturation in males was found for the start of crypt formation of the maxillary permanent canines and the maxillary second premolars, and for the start of mineralization of the maxillary permanent canines.

The data provide a tool by which chronological age can be assessed of *Macaca fascicularis* monkeys between 30 and 80 weeks of age. Due to an interphase of about one year without significant developmental features in the dentition, age assessment based on tooth development cannot be performed from about 80 to 130 weeks of age. Age assessments are again possible for the period between 130 and 150 weeks of age. However, in this period the reliability of the data is lower due to larger time intervals and standard deviations.

2.2 Introduction

The crab-eating monkey (*Macaca fascicularis*) is often used as a model for human developmental studies, especially in those dealing with growth and development of the craniofacial complex. In this type of research, development of the dentition is often a more reliable indicator of general development than the chronological age, which is often unknown.

For the infant *Macaca fascicularis*, the relation between development of the dentition and chronological age has not been established. Data on the development of the dentition of *Macaca mulatta* or data based on tooth emergence such as the number of the teeth present in the mouth, are often used to estimate the age of young *Macaca fascicularis* (Spiegel 1934; Hurme and Van Wagenen 1961; Cheverud 1981; Nanda *et al.* 1983, 1990; Van Houte *et al.* 1985; Lüder 1985), but the application of data from one species to another species is not desirable.

Assessment of age based on developmental dental characteristics derived from radiographs has the advantage that intra-osseous tooth formation can be included. Tooth formation is a progressive and continuous process which is said to be independent from local environmental factors (Bowen and Koch, 1970; Prahl-Andersen and Van der Linden, 1972).

Our purpose is to describe the development of the dentition in *Macaca fascicularis* of known age.

2.3 Materials and methods

Eight male and five female infant *Macaca fascicularis* monkeys with known background and dates of birth were available. At the start of the observation period, all animals had a complete deciduous dentition and normal occlusal relationships (neutro-occlusion) in both the posterior and the anterior regions.

The animals were housed in the Central Animal Laboratory of the University of Nijmegen and received a standard diet of wet compressed pellets and drinking water *ad libitum*. They were studied continuously from about 27 to 150 weeks of age, which is about one year after the first permanent molars were fully in occlusion.

Standardized lateral cephalometric head-films under general anaesthesia were made initially every three weeks and, after the maxillary first permanent molars had attained the level of the occlusal plane, every six weeks. General anaesthesia was produced with 10 mg/kg Ketamine (Nimatek^R, A.U.V. Cuijk, The Netherlands) and 0,1 ml Thalamonal^R (Janssen Pharmaceutica, Beerse, Belgium) and 0,2 mg Atropine (A.C.F. Pharma B.V. Maarssen, The Netherlands) administered intramuscularly. The cranium was fixed in a cephalostat with two ear-pieces and an orientation pin between the mandibular central incisors.

The central beam of the X-ray machine (Philips Practix^R, The Hague, The Netherlands) was orientated perpendicular to the mid-sagittal plane of the cranium and to the film. The distance between the X-ray focus and the midsagittal plane was 4.5 m and the distance between the latter and the X-ray film was 9 cm. The radiographs were made with 70 kV, at 20 mA and 8 sec exposure time. After the maxillary first permanent molars had reached the level of the occlusal plane the exposure time was increased to 12 sec. All headfilms were taken with the dentition in occlusion.

Intra-oral inspection was performed each time a radiograph was taken in order to record tooth emergences. On the radiographs, three developmental stages could be observed clearly.

1. *First sign of crypt formation* (in the maxilla: permanent canines, first and second premolars and third permanent molars; in the mandible: permanent canines, first and second premolars, second and third permanent molars).
2. *First sign of tooth mineralization* (in the maxilla: permanent canines and second permanent molars; in the mandible: permanent canines, first and second premolars and second permanent molars).
3. *Tooth crown completion* (in the mandible: first permanent molar).
4. *Tooth emergence* (recorded by intra-oral inspection; in both jaws: first permanent molars and central and lateral permanent incisors).

All radiographs were scored twice by the same author with an interval of at least one week. The age at which each developmental stage was scored for the first time was recorded. The mean of the two observations for each stage was used for further calculations. Mean age and standard deviation were calculated for all animals together and for males and females separately. Student's t-test was used to explore possible sex-differences.

2.4 Results

The first signs of crypt formation (Table 2-1) were noted for the mandibular and maxillary permanent canines at week 31.2 ± 3.7 and week 33.4 ± 4.8 respectively and for the first mandibular premolars at week 35.6 ± 4.1.

Table 2-1: *Start of crypt formation.*
Age in weeks (means and standard deviations) at which the first radiograph showing a crypt was taken.
*Sex difference: * = 0.01 ≤ p < 0.05; ** = p < 0.01.*

Tooth	female			male			overall		
	N	mean	SD	N	mean	SD	N	mean	SD
C inf	5	32.9	4.3	8	30.0	2.9	13	31.2	3.7
C sup	5	37.9*	3.4	8	30.6*	2.2	13	33.4	4.8
P1 inf	5	37.0	6.9	8	34.7	2.9	13	35.6	4.1
P1 sup	4	40.6	8.9	8	41.5	6.4	12	41.2	7.1
P2 inf	4	51.1	3.9	8	48.4	3.7	12	49.3	3.6
M2 inf	5	50.5	5.0	8	50.3	7.2	13	50.3	6.3
P2 sup	4	60.0**	2.0	7	53.4**	3.2	11	55.8	3.4
M3 sup	2	143.0	-	5	138.5	13.2	7	139.7	11.5
M3 inf	2	143.0	-	6	138.7	14.4	8	139.8	12.2

A statistically significant difference between the two sexes was found in the first appearance of the crypts of the maxillary permanent canines ($p < 0.05$); they showed up first in males. The crypts of the maxillary first premolars appeared on the radiographs at week 41.2 ± 7.1 and those of the mandibular second premolars at week 49.3 ± 3.6. The first appearance of the mandibular second permanent molar crypts was noted at week 50.3 ± 6.3

and of maxillary second premolars at week 55.8 ± 3.4. For the latter a sex difference was found. The crypt formation of the maxillary second premolars started earlier in the male than in the female monkeys ($p < 0.01$). The crypts of the maxillary and mandibular third molars appeared around the same time at week 139.7 ± 11.5 and 139.8 ± 12.2 respectively.

Mineralization (Table 2-2) was first noted for the mandibular permanent canines at week 41.7 ± 3.5 approximately 10 weeks after the first appearance of their crypts.

Table 2-2: *Start of mineralization.*
Age in weeks (means and standard deviations) showing the first radiographically visible sign of mineralization.
*Sex difference: * = 0.01 ≤ p < 0.05.*

Tooth	female			male			overall		
	N	mean	SD	N	mean	SD	N	mean	SD
C inf	5	43.0	3.9	8	40.9	3.6	13	41.7	3.5
C sup	5	50.7*	7.8	8	38.9*	8.0	13	43.5	9.6
P1 inf	5	52.4	4.4	8	46.1	9.0	13	48.5	7.4
M2 inf	4	58.8	8.2	7	60.5	6.4	11	59.5	6.8
P2 inf	4	63.0	3.8	8	62.2	5.4	12	62.5	5.2
M2 sup	4	63.8	3.8	8	61.4	3.8	12	62.5	3.5

The maxillary permanent canines showed mineralization also about 10 weeks after the first appearance of their crypts, at week 43.5 ± 9.6. Mineralization was significantly earlier in males than in females ($p < 0.05$). For the mandibular first premolars and second permanent molars mineralization was first noted at week 48.5 ± 7.4 and 59.5 ± 6.8 respectively, which was 12.9 and 9.2 weeks respectively after their crypt formation was detected. Thereafter, the mineralization of the mandibular second premolars and the maxillary second permanent molars appeared about the same time at week 62.5 ± 5.2 and 62.5 ± 3.5 respectively.

Crown completion of the mandibular first permanent molars was seen at week 44.5 ± 3.9 (Table 2-3).

Table 2-3: *Crown completion.*
Age in weeks (means and standard deviations) at which crown completion could be detected for the first time.

Tooth	female			male			overall		
	N	mean	SD	N	mean	SD	N	mean	SD
M1 inf	5	43.9	4.9	8	44.9	3.5	13	44.5	3.9

The emergence (Table 2-4) of the mandibular first permanent molars was observed at week 70.1 ± 6.5 and that of the maxillary first permanent molars at week 78.4 ± 6.2. In this respect, the mandibular permanent molars preceded the maxillary ones by about 8 weeks. At the end of the observation period, all central and lateral permanent incisors had emerged through the oral mucosa in a time span of 14 weeks (from week 129.9 ± 9.9 to week 143.7 ± 11.8).

Table 2-4: *Emergence.*
Age in weeks (means and standard deviations) at which emergence through the oral mucosa was observed.

Tooth	female			male			overall		
	N	mean	SD	N	mean	SD	N	mean	SD
M1 inf	3	69.5	4.6	6	70.4	5.9	9	70.1	6.5
M1 sup	3	76.0	4.6	6	79.7	5.4	9	78.4	6.2
I1 inf	3	132.5	8.5	6	128.7	11.1	9	129.9	9.9
I1 sup	3	140.3	4.2	6	130.0	12.2	9	133.4	11.2
I2 inf	3	140.3	4.2	6	133.7	12.7	9	135.9	11.4
I2 sup	3	148.3	9.9	4	140.3	15.7	7	143.7	11.8

The data can be divided in two parts, an early infant period and a late infant period with an interphase of nearly one year. The diagram (Fig. 2-1) visualises the sequence of developmental stages.

The diagram provides a tool to assess the chronological age of a specimen on basis of its tooth development. For that purpose the radiograph of this specimen has to be compared with the diagram in order to find the best fit of the dental stages. The accuracy of this assessment depends on the one hand on the number of developmental stages involved and on the other hand on the range of variation recorded for these stages.

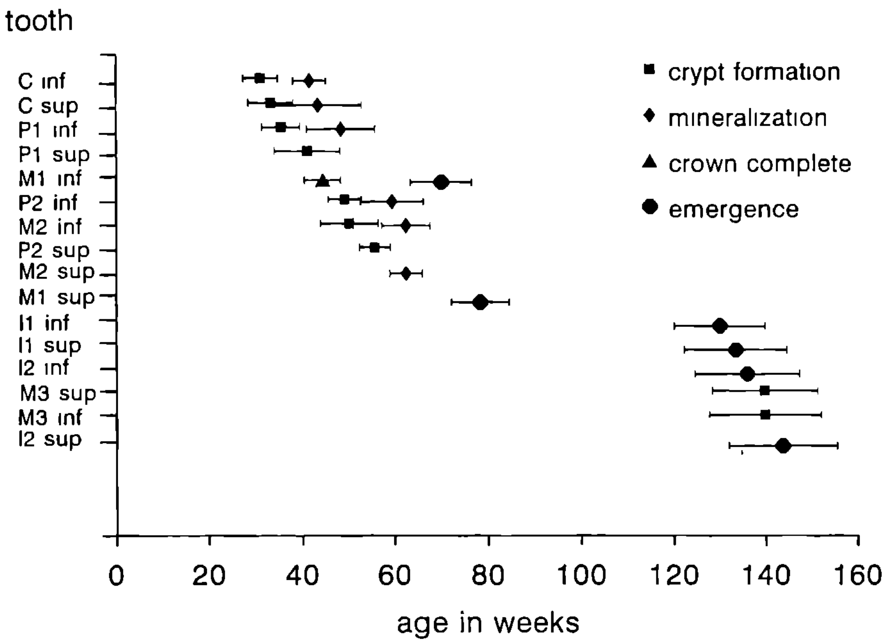

Figure 2-1: *Graphic presentation of ages (means ± 1 SD) of dental developmental stages of permanent teeth in the infant period of the Macaca fascicularis monkey. For definition of stages see text.*

2.5 Discussion

On lateral radiographs over-lap between bony structures of left and right tend to obscure the developmental stages of several teeth. Thus a period of about one year (from 80-130 weeks) passes in which no useful data can be obtained. This means that on lateral radiographs reliable data can only be obtained from an early infant period lasting from about 30-80 weeks and from a late infant period lasting from about 130-150 weeks of age. The early infant period covers a time span of about 40 weeks, and includes most of the developmental stages. The spacing between the mean ages for the different developmental stages is more than 5 weeks only in few cases. This means that in this early infant period, accurate age assessments can be performed. In the interphase, no data on tooth development are available.

For the late infant period, the age assessments have to be based on the start of permanent third molar crypt formation, which shows a large biologic variation, and on the emergence of the permanent incisors. The emergence of the permanent incisors is dependent on their biological development, but also depends in some extent on the actual moment of exfoliation of the deciduous predecessor. Besides, the observations in the late infant period were carried out every six weeks. The combination of these factors may explain the relative inaccurate findings for the late infant period.

Bowen and Koch (1970) also reported on tooth development in *Macaca fascicularis*. Their data show systematic higher ages for all radiographically recorded developmental stages than those found in the present study. This difference is probably due to our radiographic observations in the early infant period being carried out every three weeks and theirs only every two months, which causes a systematic overestimation of the age at which a certain phenomenon takes place. On the other hand, our findings on the intra-oral observations on emergence of permanent teeth in the late infant period show systematic higher values than theirs, possibly caused by the soft consistency of the diet of the animals used in the present study, which might have delayed the exfoliation and subsequent shedding.

Sex differences with an earlier development in males than in females were found for the start of crypt formation and the onset of mineralization of the maxillary permanent canines and in the start of crypt formation of the maxillary second premolars. The cause of these sex differences is not known, but might be related to the final dimensions of the teeth, as it is well known that in *Macaca fascicularis* the permanent canines in the males become considerably larger than in the females. This means that the assessments in the early infant period become more accurate for the stages of the permanent upper canines and the permanent upper second premolars if the sexes are separated.

The earlier development of certain teeth in males than in females appears not to be generally applicable to all Macaque *species*. Swindler and co-workers, in their study on *Macaca nemestrina* report earlier tooth development in females than in males (Swindler *et al.*, 1982; Swindler, 1985).

Some authors (e.g. Michejda, 1978; Cheverud, 1981; Lüder, 1985) consider that tooth development characteristics are unreliable for age assessment. However they based their conclusions on studies which recorded only the numbers of emerged permanent teeth. As is also shown here, the moment of emergence shows large biological variation. According to Demirjian (1978), the accuracy of dental age assessment increases considerably if developmental stages derived from lateral radiographs are included.

In conclusion, this study shows that lateral radiographs can be used as a valuable tool in the age assessment of *Macaca fascicularis* monkeys in the early infant period. Also in the late infant period lateral radiographs in combination with intra-oral inspection enables an estimation of the age of these monkeys.

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Chapter 3

A longitudinal cephalometric study of dento-facial growth in juvenile crab-eating monkeys (*Macaca fascicularis*) a radiographic study

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3.1 Summary

The aim of the present study was to describe dento-facial growth and development in the juvenile *Macaca fascicularis*. Six males and one female laboratory-born monkeys were followed from 29 to 143 weeks of age. Tantalum implants in bones and teeth were used as markers. Standardized lateral cephalometric radiographs were taken every three weeks and, after the first permanent molars had reached the occlusal plane, every 6 weeks. Growth data were obtained by analysing the changes in relation to the frontal bone implant and the Anterior Cranial Base line and also in relation to implants placed in the jaws.

The rate of skeletal and dental changes was large at the start of the study and decreased as growth proceeded. In almost every interval the recorded maxillary vertical dimensions increased less than the horizontal ones, while the mandibular vertical dimensions increased more than the horizontal ones. The dentition in the maxilla showed a continuous anterior displacement in respect to the bone, while in the mandible the dentition moved with the bone. This resulted in a stable pattern of occlusion.

The results suggest that the dento-facial growth and development in the juvenile *M. fascicularis* and in humans have many points in common, and therefore, *M. fascicularis* appears to be a good model for further studies on the regulation of the processes involved.

3.2 Introduction

The development of skeletal morphology and physiology of the dento-facial complex probably is the result of an interplay between skeletal parts and dentition. The final outcome of this interplay depends on the mutual influences of the composing parts. On the one hand skeletal development provides the spatial circumstances in which the dentition can develop, and on the other hand the development of the dentition may play a role in the development of the alveolar bone and its surrounding structures and in the growth of jaws (Petrovic *et al.*, 1975; Stutzmann and Petrovic, 1976; Petrovic and Stutzmann, 1977; Brace, 1977; Van der Linden, 1977, 1982, 1986). The role of occlusion and interdigitation of the dentition of both jaws in the skeletal development is less obvious, but studies on human material of different ages led to the hypothesis that interdigitation plays a guidance role in normal human dento-facial growth and development (Brace, 1977; Van der Linden, 1986). The general idea of this hypothesis is that once a normal buccolingual interdigitation is attained, the development of the maxillary dental arch and adjacent structures is regulated by the interlocking of the cusps to follow the changes in the mandibular arch. Van der Linden called this regulation system the "rail mechanism" (Van der Linden, 1986).

Also observations in non-human primates point in the direction of a functioning rail mechanism. Most of this work has been performed in *M. mulatta* and *M. nemestrina* (Elgoyhen *et al.*, 1972; Swindler *et al.*, 1973; McNamara Jr and Graber, 1975; McNamara Jr *et al.*, 1976; Bravo *et al.*, 1989; Nielsen *et al.*, 1989). Baume and Becks (1950) and Elgoyhen *et al.*, (1972) found that in juvenile *M. mulatta*, the occlusal relation was maintained in a changing maxillo-mandibular relationship. This was confirmed by McNamara *et al.*, (1976) in *M. mulatta* in the age from 6 months to 6 years and also by Swindler *et al.*, (1973) in a study on *Papio cynocephalus* and *M. nemestrina* from 3 months to 3 years of age.

In recent years *M. fascicularis* is also been used in studying dento-facial growth. Nanda *et al.* (1987) reported corresponding findings in a study on older *M. fascicularis*, from 3 to 5 years of age. However, a description of the normal growth and development of the dento-facial complex and the interdigitation in juvenile *M. fascicularis* is lacking up to now.

In order to fill up this gap in our knowledge, this study is conducted, aiming at the description of the normal dento-facial growth and development of juvenile *M. fascicularis* and the evaluation of the usefulness of this animal as a model for further studies on regulation processes in dento-facial growth and development.

3.3 Methods

Six male and one female laboratory-born crab-eating monkeys (*Macaca fascicularis*) were used in this study. The sexes were combined in the analysis of the data. This is legitimate as sexual dimorphism in *Macaca spec.* becomes only apparent after the age of approximately three years and therefore could be neglected for the present study (Gavan & Swindler, 1966; Swindler *et al.*, 1973; Swindler & Sirianni, 1973; McNamara *et al.*, 1976; Sirianni & Van Ness, 1978; Sirianni, 1985). All animals showed a neutro-occlusion of the posterior teeth and an occlusion in the frontal region between a nearly end-to-end to a slight overjet and overbite. None of the animals had a malocclusion or a skeletal deviation.

At the start of the study, the mean age of the animals was 29 weeks. At that time the onset of crypt formation of the mandibular permanent canines had just started and the second deciduous molars had emerged recently (Ostyn *et al.*, 1994). All animals were followed until 143 weeks of age except for one male, which accidentally died at the age of 80 weeks. The animals were housed in the Central Animal Laboratory of the University of Nijmegen and they received a standard diet of wet compressed pellets and drinking water *ad libitum*.

At the start of the study, Tantalum implants (Ole Dich, Hvidovre, Denmark) measuring 1.2 mm in length and 0.5 mm in width were inserted as bone markers in each monkey. Prior to implantation the animals were anaesthetized with 10 mg/kg Ketamine (Nimatek^R, A.U.V., Cuijk, The Netherlands). Subsequently 0.1 ml Thalamonal^R (Janssen Pharmaceutica, Beerse, Belgium) and 0.25 mg Atropine (Atropine Sulphate, A.C.F., Pharma

B.V., Maarssen, The Netherlands) were administered intra-muscularly. Skin incisions were made along the lower border of the mandible and, after preparing a small hole, two implants were hammered into the bone (Björk, 1955, 1968). The same procedure was followed for inserting implants in the frontal bone. In addition, implants were inserted in the palate through the mucosa (Fig. 3-1).

As soon as possible after emergence, the deciduous and permanent molars were provided with Tantalum balls, with a diameter of 0.5 mm. To that end a small hole was prepared in the buccal surface in which the implant was secured with composite material.

Standardized lateral cephalometric radiographs were taken at regular intervals, initially every three weeks but, after the maxillary first permanent molars had attained the level of the occlusal plane, the frequency was reduced to once every six weeks. The radiographs were taken with the teeth in occlusion.

The central beam of the X-ray machine (Philips Practix^R, The Hague, The Netherlands) was orientated perpendicular to the midsagittal plane of the cranium and the film. The distance between the X-ray focus and the midsagittal plane was fixed at 4.5 m and the distance between the latter and the X-ray film at 9 cm. The radiographs were made with 70 kV at 20 mA and 8 sec exposure time. After the maxillary first permanent molars had reached the level of the occlusal plane the exposure time was increased to 12 sec. The radiographs were instantly developed and compared with the one of the previous session. If a radiograph showed that a bone or tooth implant had become loose, a new one was inserted immediately, and the radiographic procedure was repeated.

Growth and displacements were analyzed in a constructed Cartesian coordinate system, which is comparable to the coordinate system used by McNamara *et al.* (1976) and Nanda *et al.* (1987) (Fig. 3-1). On the last collected lateral radiograph, the direction of the functional occlusal plane was determined using the mesial anatomic contact points of the mandibular first and second deciduous molars. A line parallel to the occlusal plane, but out of the measuring area was constructed which served as X-axis. The origin was defined as the point of intersection between the X-axis and the line through the frontal bone implant and the floor of Sella turcica (Anterior Cranial Base line). A line perpendicular to the X-axis through the origin served as Y-axis.

All preceding radiographs were superimposed on the frontal bone marker and the Anterior Cranial Base line, and the same coordinate system served as a reference frame. This means that skeletal and dental changes and displacements of the maxillary and mandibular structures could be quantified in relation to the position of the frontal bone implant. Also mutual distances between other implants could be calculated. The coordinates of the landmarks and the bone and tooth implants were digitized with an electronic measuring table.

The following measuring points were used (Fig. 3-1):

1. frontal bone implant (FB)
2. anterior maxillary bone implant (AU)
3. posterior maxillary bone implant (PU)
4. tooth implant in the maxillary first deciduous molar (TU)
5. tooth implant in the mandibular first deciduous molar (TL)
6. infradentale = junction point between the anterior outline of the mandibular central incisor and the adjacent alveolar bone (ID)
7. menton = lowermost point of the symphysis (Me)
8. anterior mandibular bone implant (AL)
9. posterior mandibular bone implant (PL)
10. gonion = construction point located on the intersection of the bisector of the angle of the posterior ramal plane and the mandibular plane, and the mandibular contour (Go)
11. condylion = the most postero-superior point on the condyle (Co)
12. symphysial point = construction point on the middle of a line between infradentale (ID) and menton (Me) (McNamara and Bryan, 1987) (Sy).

Nearly all growth parameters as calculated from these points are related to bone or tooth implants. Although those markers are placed as accurate as possible in the same regions, they cannot be considered as identical for the different animals. This means that for the description of growth not the distances themselves can be used, but that the increments, i.e. the changes in distances in time have to be considered.

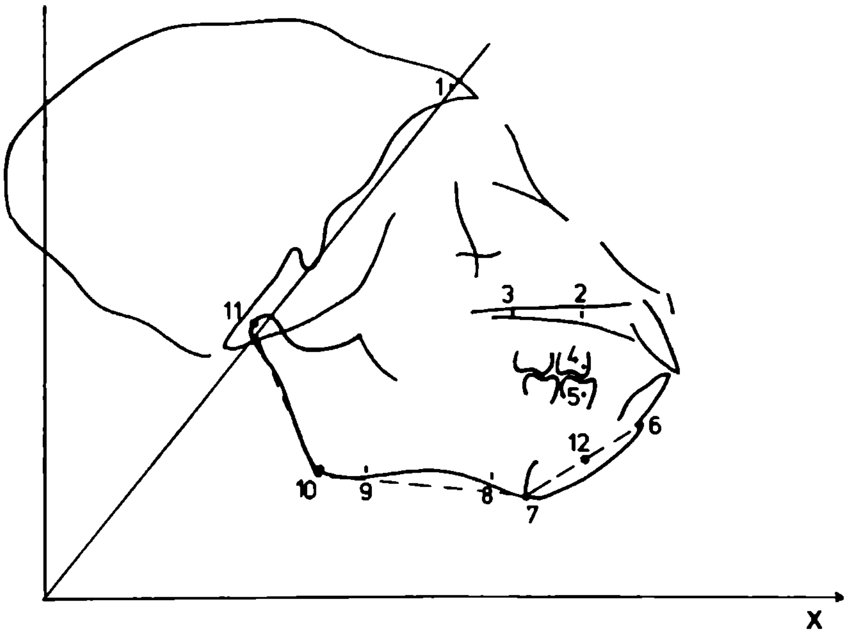

Figure 3-1: *Schematic drawing of the skull of a Macaca fascicularis and the cartesian coordinate system based on the Anterior Cranial Base line and the functional occlusal plane.*
The landmarks and the positions of the implants in bones and teeth are indicated. For definitions: see text.

The use of increments has also the advantage that in case an implant was replaced, the analysis of the growth could easily be continued.

For the analysis of the changes of the maxillary structures relative to the frontal bone implant increments in vertical and in horizontal direction of the distances FB-AU and FB-PU were calculated. Facial height changes were studied by the increments of distance FB-Me in the vertical direction.

Changes in position of the maxillary dentition within the maxillary bone were quantified by calculating increments of distance PU-TU in horizontal direction. For the study of changes in position of the maxillary structures relative to the mandible, increments of the distances PU-AL and PU-PL were calculated in vertical and horizontal direction.

In order to study changes in the position of the mandible relative to the frontal bone implant increments of the distances FB-AL and FB-PL were calculated in vertical and horizontal direction. Furthermore the increments of the overall length of the mandible (Co-Sy) and the changes in the gonial angle (Me-Go-Co) were determined.

To describe the changes in the position of the mandibular dentition in relation to the mandibular bone, increments of distance PL-TL were calculated in horizontal direction.

Changes in the relationship between the two dental arches were studied by calculating the increments of distance TU-TL in horizontal direction.

For the interpretation of the findings, the total period under study (29-143 weeks of age) was divided in five sub-periods: an initial one covering the first 10 weeks and four sub-periods of 26 weeks each. In cases of comparison of two parameters, the differences were statistically analyzed using the paired t-test at the 0.05 level.

The total error of the method which is composed of the positioning and measurement error, was determined by measuring 5 sets of independent radiographs from two animals of 86, and two other animals of 110 weeks of age. Between the exposures the animals were removed and replaced in the cephalostat. The measurement error was studied by double determination of all variables recorded in a longitudinal series of one monkey.

3.4 Results

A suitable description of the errors could be obtained by specifying the error in vertical and in horizontal direction, separately for all distances and increments used. In total eight categories of errors were analyzed. Most of the errors were 20 μm or less. Only the errors in the distances and increments in horizontal direction in relation to the image of the frontal bone implant showed comparatively high values of 38 and 60 μm respectively. This error was mainly caused by positioning the animal in the cephalostat and by inaccuracies associated with the determination of the Anterior Cranial

Base lıne Partıcularly the latter can effect markedly the error of the method ın horızontal dırectıon

The total error of the gonıal angle was found to be 1 1° and that of the mandıbular length 32 μm, whıch was consıdered to be acceptable The measurement error ın the ıncrements was calculated as duplıcate error and varıed for all categorıes between 12 and 18 μm The measurement error ın the gonıal angle showed a value of 0 7°

Table 3-1: *Mean ıncrements ± SEM ın μm per week over each perıod, of the dıstances between the maxıllary ımplants and the frontal bone ımplant, and between a maxıllary tooth and the posterıor maxıllary ımplant*

Age ın weeks	FB-AU		FB-PU		PU-TU	
	Horızontal	Vertıcal	Horızontal	Vertıcal	Horızontal	Vertıcal
29 - 39	102 ±24	54 ±11	98 ±25	68 ±11	59 ± 8	66 ± 9
39 - 65	64 ± 7	42 ± 8	62 ± 7	50 ± 8	36 ± 3	40 ±42
65 - 91	71 ±14	31 ± 4	69 ±11	43 ± 4	44 ± 3	30 ± 4
91 - 117	45 ± 8	35 ± 8	43 ± 9	43 ± 6	21 ± 2	29 ± 4
117 143	57 ± 8	34 ± 3	55 ± 8	40 ± 4	18 ± 5	32 ± 3
39 - 143	60 ± 7	35 ± 4	58 ± 7	43 ± 5	29 ± 1	31 ± 2

The horızontal dısplacement of the maxıllary structures relatıve to the frontal bone ımplant (FB-AU and FB PU) was relatıvely large ın the first perıod wıth a mean ınıtıal rate of about 100 μm per week Thereafter the dısplacements were smaller and varıed between 40 μm and 70 μm per week (Table 3-1) The dıfferences between both parameters were never statıstıcally sıgnıficant In vertıcal dırectıon, the dısplacements of the maxıllary structures were consıstently smaller than ın horızontal dırectıon Theır rates seemed to decrease gradually ın the first three perıods Thereafter rather constant dısplacement rates were found The vertıcal dısplacement of the anterıor regıon (AU) was systematıcally, but not sıgnıficant, smaller than of the posterıor part (PU)

For the main period the mean values were 35 ± 4 versus 43 ± 5 μm per week respectively, which suggested a counter-clockwise rotational tilting of the maxillary structures (Fig. 3-2).
The maxillary first deciduous molar showed a continuous anterior and inferior displacement relative to the posterior maxillary implant (PU-TU). The horizontal and vertical component of this variable showed a mean initial increase of about 60 μm per week. This rate decreased during the observation period.

The distances from the frontal bone implant to the mandibular bone implants (FB-AL and FB-PL) measured in an horizontal direction showed a pattern comparable to the parameters FB-AU and FB-PU. However, the mean increments for the mandibular implants were considerably larger than those of the maxillary ones (Table 3-1, 3-2).

Initially they amounted about 160 ± 30 μm per week, in the following periods gradually decreasing to about 60 ± 10 μm per week. This indicates an anterior displacement of the mandible with respect to the maxillary structures (see also Table 3-4). The rate of the inferior displacement of both mandibular implants tended to decrease gradually during the first three periods and remained rather constant thereafter. Like the posterior maxillary implant (PU), the posterior mandibular implant (PL) tended to undergo a larger vertical displacement than the anterior one. The differences, however were statistically not significant, but suggest that, also for the mandible a counterclockwise, rotational displacement takes place (Fig. 3-2).

The mandibular dentition, as represented by the tooth implant in the mandibular first deciduous molar, moved on the average, slightly distally relative to the mandibular basal bone during the whole observation period (PL-TL). The rate of the vertical migration of the tooth relative to the mandibular bone was about twice that found for the maxilla (Table 3-1, 3-2).

The growth of the mandible (Co-Sy) decreased in the first three periods and remained approximately constant thereafter (Table 3-3). The gonial angle (Me-Go-Co) appeared to be more or less constant during the main period.

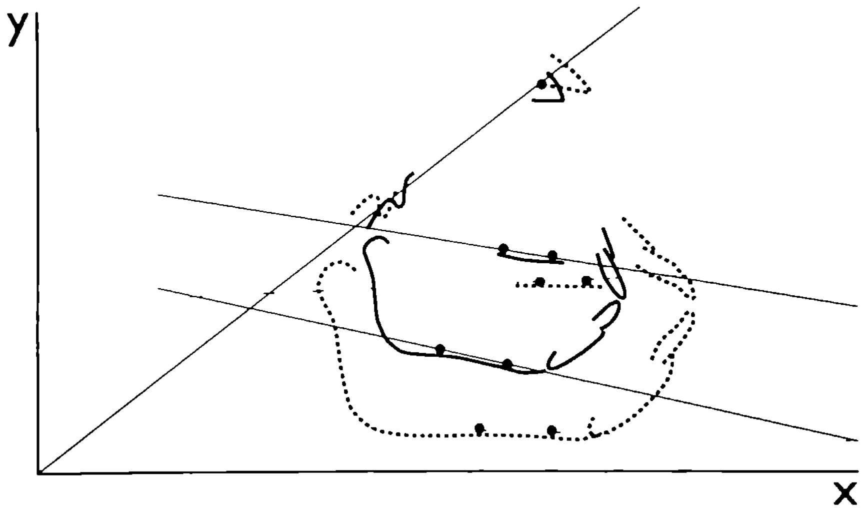

Figure 3-2: *Schematic presentation of tracings at the start and the end of the study, illustrating the counterclockwise rotation of the maxilla and the mandible during growth*

Table 3-2: *Mean increments ± SEM in µm per week over each period of the distances between mandibular implants and the frontal bone implant, and between a mandibular tooth and the posterior mandibular bone implant*

Age in weeks	FB-AL Horizontal	FB-AL Vertical	FB-PL Horizontal	FB-PL Vertical	PL-TL Horizontal	PL-TL Vertical
29 - 39	164 ±34	189 ±24	154 ± 32	221 ±22	-9 ±10	111 ±15
39 65	99 ±15	146 ±15	94 ± 14	170 ±17	-10 ± 6	88 ± 9
65 - 91	102 ±15	101 ± 6	100 ± 16	125 ± 7	-13 ± 4	74 ± 8
91 - 117	57 ±12	105 ±10	52 ± 11	110 ±10	-9 ± 4	43 ± 4
117 - 143	72 ±10	95 ± 5	73 ± 10	110 ± 6	9 ± 7	47 ± 7
39 - 143	89 ± 8	110 ± 4	80 ± 8	127 ± 4	-6 ± 3	62 ± 3

Table 3-3: *Mean increments ± SEM in μm per week over each period of the overall length of the mandible (Co-Sy) and the total facial height (FB-Me) and in degrees ± SEM per week over each period of the gonial angle.*

Age in weeks	Co-Sy	Me-Go-Co	FB-Me
29 - 39	250 ± 20	-1.14 ± 1.74	198 ± 26
39 - 65	200 ± 19	-0.70 ± 0.26	147 ± 16
65 - 91	150 ± 10	-0.57 ± 0.29	112 ± 5
91 - 117	154 ± 10	0.68 ± 0.28	119 ± 9
117 - 143	140 ± 18	0.48 ± 0.32	99 ± 6
39 - 143	160 ± 9	-0.06 ± 0.14	117 ± 4

The total face height, expressed as the vertical distance from the frontal bone implant to menton (FB-Me), increased during the whole observation period. During the first two periods the rate decreased; thereafter the increments remained more or less stable, fluctuating between 100 and 120 μm per week (Table 3-3).

Comparison of the data obtained from the mandible and the maxilla confirmed that the mandible moved faster than the maxilla in the anterior as well as in the inferior direction (PU-AL and PU-PL). These differences were significant for most sub-periods and for the main period, but decreased during the observation period. The horizontal displacement of the tooth markers in the mandible and the maxilla (TU-TL) was about identical during the whole observation period and therefore the occlusion of these teeth did not seem to alter (Table 3-4).

3.5 Discussion

Dento-facial growth patterns of *M. mulatta*, and *M. nemestrina* have extensively been described and they appear to be comparable and qualitatively similar (McNamara & Graber, 1975; McNamara *et al.*, 1976; Sirianni & Van Ness, 1978; Sirianni & Swindler, 1979; Sirianni *et al.*, 1982).

Table 3-4: *Mean differences in increments ± SEM in μm per week over each period of the distances between bone or tooth implants in the mandible and the maxilla. * = differences > 0; p < 0.05.*

Age in weeks	PU-AL		PU-PL		TU-TL
	Horizontal	Vertical	Horizontal	Vertical	Horizontal
29 - 39	66 ±11*	120 ±21*	56 ± 8*	152 ± 21*	0 ± 10
39 - 65	37 ± 9*	95 ± 8*	32 ± 9*	120 ± 10*	6 ± 3
65 - 91	33 ± 6*	58 ± 7*	31 ± 6*	83 ± 6*	0 ± 2
91 - 117	14 ± 3*	62 ± 5*	8 ± 4	67 ± 4*	-4 ± 3
117 - 143	17 ± 4*	56 ± 5*	18 ± 4*	70 ± 3*	-9 ± 10
39 - 143	25 ± 3*	66 ± 1*	22 ± 2*	84 ± 2*	-1 ± 2

Nanda *et al.* (1987) described the dento-facial growth of *M. fascicularis* from 3 to 5 years of age. The present study covers the period from 29 to 145 weeks of age, and therefore it can be considered as a supplement to the one by Nanda and co-workers (1987). The findings of the present study are concurrent with theirs, and the combination of both studies revealed a continuously decreasing growth rate of the dento-facial complex in *M. fascicularis* from 29 weeks to five years of age. A similar decrease in growth rate was also shown in *M. nemestrina* and *P. cynocephalus* from three months to three years (Swindler *et al.*, 1973).

The horizontal growth and development of the jaws and their spatial relation in *M. fascicularis* show the same characteristics as described in *M. nemestrina* and *P. cynocephalus* by Swindler *et al.* (1973), in juvenile *M. mulatta* by Elgoyhen *et al.* (1972) and in older *M. fascicularis* by Nanda *et al.* (1987). Also the vertical development of the dento-facial complex of *M. fascicularis*, which was characterized by a forward and downward displacement of the maxillary structures and an increase of the height of the alveolar process in the posterior region of the mandible is concomitant with findings in *M. mulatta* (Elgoyhen *et al.*, 1972; McNamara *et al.*, 1976 and Bravo *et al.*, 1989) and in *M. fascicularis* at later developmental stages (Nanda *et al.*, 1987).

The maxillary structures and the mandible both show a tendency to a counterclockwise rotational displacement, which is in accordance with findings described by Elgoyhen *et al.* (1972), McNamara *et al.* (1976), Nanda *et al.* (1987) and Nielsen *et al.* (1989). Also in humans rotations of both jaws during growth have been described (Björk & Skieller, 1972, 1977, 1983). However, in contrast to *Macaca spec.*, the maxillary and mandibular rotations in humans are mostly clockwise.

In the first half of the observation period the growth rate of the overall length of the mandible decreased continuously. In the second half the increase in mandibular length was more or less constant which is in accordance with the findings of Swindler (1973) in juvenile *M. nemestrina*. Analysis of gonial angle changes revealed only minor changes, but no definite conclusions could be drawn due to large measurement errors and considerable individual variation. In *M. nemestrina* and *P. cynocephalus* variability in the mandibular shape was reported by Swindler *et al.* (1973) and *M. mulatta* by Elgoyhen *et al.* (1972). Sirianni *et al.* (1982) noted also minor changes in the form of the mandible in *M. nemestrina* during growth.

Although both jaws were growing in horizontal direction at different rates, the occlusion did not alter which is in accordance to the findings of Baume & Becks (1950), Elgoyhen *et al.* (1972), Swindler *et al.* (1973), McNamara *et al.* (1976) and Nanda *et al.* (1987). This might be explained by the assumption of Elgoyhen *et al.* (1972) that the steeply inclined cuspal planes of the permanent molars in *M. mulatta* and *M. nemestrina* and older *M. fascicularis* are responsible for the maintenance of such a stable occlusion in monkeys.

In 1977 Brace postulated that interdigitation is also an important factor in the development of the pre-adolescent face in humans. Later, Van der Linden (1986) elaborated this hypothesis further, stating that once a normal buccolingual interdigitation is attained the development of the maxillary dental arch and adjacent structures is guided by the mandibular dental arch by interlocking of the cusps of both jaws, the so-called "rail mechanism". The finding that the occlusion in juvenile *M. fascicularis* remains stable, while the jaws show different growth rates, seems to support that hypothesis. However, an experimental approach is indicated to obtain conclusive evidence for the hypothesis and to get more indications whether the maxillary or the mandibular arch plays the leading role.

3.6 Conclusions

1. *M fascicularis* is comparable to other *Macaca species* as far as growth of the dento-facial complex is concerned.
2. *M. fascicularis* is suited as an experimental model for the study of human dento-facial growth and development.
3. Further experimental research is indicated to get more insight in the role of interdigitation in the regulation of the horizontal maxillo-mandibular development in *M fascicularis*.

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Chapter 4

The role of interdigitation in sagittal growth of the maxillo-mandibular complex in *Macaca fascicularis*

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4.1 Summary

The role of the interdigitation of posterior teeth in maxillo-mandibular growth and development was studied longitudinally in *Macaca fascicularis* monkeys.

Fourteen monkeys were divided into a control group (n = 7) and an experimental group (n = 7). At the start of the study, the mean age of the animals was 29 weeks. At that stage the interdigitation in the experimental group was eliminated by grinding the cusps of the molars and canines. The animals were followed until 143 weeks of age and studied with the aid of tantalum implants and lateral radiographs.

The findings indicated that elimination of the interdigitation resulted in a deviating antero-posterior relationship between the jaws and a significant inhibition of the vertical growth of the maxilla in the second half of the experimental period, while total face height was not noticeably affected. As a result a more prognathic mandible and a more mesial occlusion developed.

It can be concluded that the interdigitation plays a role in the regulation of vertical and antero-posterior facial growth and constitutes an important factor in the jaw relation in *Macaca fascicularis* monkeys.

4.2 Introduction

The antero-posterior and transverse development of the jaws in humans is assumed to be, at least partly, coordinated by the occlusion and interdigitation of the posterior teeth. This view emerged from physical, anthropological as well as clinical considerations[1,2]. Further it has been suggested on a hypothetical basis that occlusion and interdigitation influence naso-maxillary and alveolar growth[3].

Various animal experiments have been performed to study the role of interdigitation in the coordination of facial growth in sagittal direction. After superior repositioning of the maxilla in *Macaca fascicularis*, Nanda and co-workers[4,5] found a reduction in growth of both jaws which led to the assumption that interdigitation played a role in maxillo-mandibular growth. Petrovic and co-workers[6,7,8], performed a variety of experiments in rats and leading to the conclusion that the occlusion is an important factor in the coordination of the lengthening of the jaws.

In experiments on *Macaca mulatta*, Sarnat[9,10] noted no significant gross difference in maxillary growth after resection of the median and transverse palatine sutures and he stated that the mandible may have guided the maxillary growth by means of the occlusion. On the other hand Kantomaa and Rönning[11] did not find evidence in experiments on rats for the assumption that the relation between the jaws is regulated by interdigitation and they stated that the mandible may be carried forward passively with the growth of the maxilla.

However, in all experimental approaches so far, the original craniofacial development has been disturbed by surgical intervention or by growth restriction or stimulation, which limits extrapolation of these findings to normal growing systems. To meet this shortcoming, in the present study the contribution of interdigitation to sagittal development of the maxillo-mandibular complex is investigated using an experimental set-up in which growth centres are not directly disturbed or affected. *Macaca fascicularis* monkeys were used since their basic plan of growth of face and cranium parallels that found in humans[12,13].

4.3 Materials and methods

Eleven male and three female laboratory-born *Macaca fascicularis* monkeys were used in this study. The animals were randomly divided in a control group (n = 7) and an experimental group (n = 7). The sexes were combined in the analysis of the data. This is legitimate as sexual dimorphism in *Macaca spec.* becomes only apparent after the age of approximately three years and therefore could be neglected for this study. All animals showed a neutro-occlusion of the posterior teeth and an occlusion in the frontal region between a nearly end-to-end to a slight overjet and overbite. None of the animals had a malocclusion or a skeletal deviation.

At the start of the study, the mean age of the animals was 29 weeks. At that time the onset of crypt formation of the mandibular permanent canines had just started and the second deciduous molars had emerged recently[14]. All animals were followed until 143 weeks of age except for one male animal from the control group, which accidentally died at the age of 80 weeks.

The animals were housed in the Central Animal Laboratory of the University of Nijmegen and they received a standard diet of wet compressed pellets and drinking water *ad libitum*.

Before the start of the study tantalum implants (Ole Dich, Hvidovre, Denmark), measuring 1.2 mm in length and 0.5 mm in width were inserted as bone markers in each monkey[15,16]. Prior to implantation the animals were anaesthetized with 10 mg/kg Ketamine (Nimatek^R, A.U.V., Cuijk, The Netherlands). Subsequently 0.1 ml Thalamonal^R (Janssen Pharmaceutica, Beerse, Belgium) and 0.25 mg Atropine (Atropine Sulphate 0.5 mg/ml, A.C.F. Pharma BV, Maarssen, The Netherlands) were administered intramuscularly. Skin incisions were made along the lower border of the mandible and, after preparing a small hole, two implants were hammered in the bone. The same procedure was followed for inserting implants in the frontal bone. Further implants were inserted in the palate through the mucosa (Fig. 4-1).

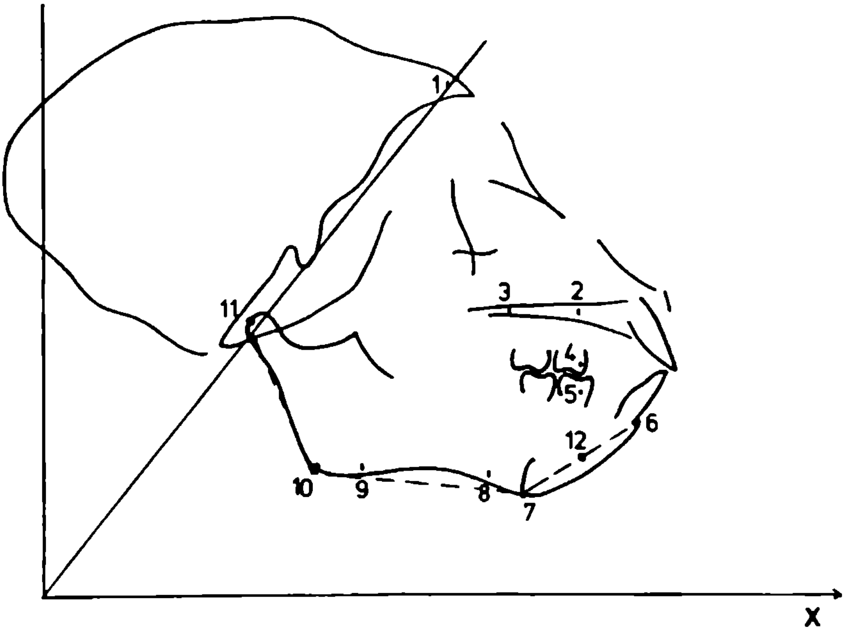

Figure 4-1: *Schematic drawing of the skull of a Macaca fascicularis and the Cartesian coordinate system defined by the Anterior Cranial Base line and the occlusal plane.*
The landmarks and the positions of the implants in bones and teeth are indicated. For definitions: see text.

As soon as possible after emergence, all deciduous and permanent molars were provided with tantalum balls, with a diameter of 0.5 mm. To that end a small hole was prepared in the buccal surface of each molar in which the implant was secured with composite material.

In the animals of the experimental group interdigitation was eliminated by grinding successively the cusps of the deciduous molars and canines and those of the first permanent molars in both dental arches until a flat surface was obtained. The grinding was carried out under general anaesthesia at the first regular session after emergence. The cusps were ground without jeopardizing the vitality of the pulp. The grinding did not affect the approximal contacts of the deciduous and permanent molars.

Initially standardized lateral cephalometric radiographs were taken every three weeks, but after the maxillary first permanent molars had attained the level of the occlusal plane the frequency was reduced to once every six weeks.

The central beam of the X-ray machine (Philips Practix^R, The Hague, The Netherlands) was orientated perpendicular to the midsagittal plane of the cranium and the film. The distance between the X-ray focus and the midsagittal plane was fixed at 4.5 m and the distance between the latter and the X-ray film at 9 cm.

The radiographs were made with 70 kV at 20 mA and 8 sec exposure time. After the maxillary first permanent molars had reached the level of the occlusal plane the exposure time was increased to 12 sec. The radiographs were taken with the teeth in occlusion.

If a radiograph showed that a bone or tooth implant had became loose, a new one was inserted immediately, and the radiographic procedure was repeated. This was necessary for 8 out of 70 bone implants and for 24 out of 84 tooth implants over the total experimental period of 2.5 years.

Growth changes and displacements were analyzed in a constructed Cartesian coordinate system, which is comparable to the coordinate system as used by McNamara and Bryan[17] and Nanda *et al.*[18] (Fig. 4-1). On the last collected lateral radiograph, the functional occlusal plane was determined using the mesial anatomic contact points of the mandibular first and second deciduous molars. A line parallel to the occlusal plane, but out of the measuring area was constructed which served as X-axis. The origin was defined as the point of intersection between the X-axis and the line through the frontal bone implant and the floor of Sella turcica (Anterior Cranial Base line). A line perpendicular to the X-axis through the origin served as Y-axis.

All preceding radiographs were superimposed on the frontal bone marker and the Anterior Cranial Base line, and the same coordinate system served as a reference frame. This means that skeletal and dental changes and displacements of the maxillary and mandibular structures could be quantified in relation to the position of the frontal bone implant. Also mutual distances

between other implants could be calculated. The coordinates of the landmarks and the bone and tooth implants were digitized with an electronic measuring table equipped with a microscope, resulting in a ten-fold magnification.
The following measuring points were used (Fig. 4-1):

1. frontal bone implant (FB)
2. anterior maxillary bone implant (AU)
3. posterior maxillary bone implant (PU)
4. tooth implant in the maxillary first deciduous molar (TU)
5 tooth implant in the mandibular first deciduous molar (TL)
6. infradentale = junction point between the anterior outline of the mandibular central incisor and the adjacent alveolar bone (ID)
7. menton = lowermost point of the symphysis (Me)
8. anterior mandibular bone implant (AL)
9. posterior mandibular bone implant (PL)
10. gonion = construction point located on the intersection of the bisector of the angle of the posterior ramal plane and the mandibular plane, and the mandibular contour (Go)
11. condylion = the most postero-superior point on the condyle (Co)
12. symphysial point = construction point on the middle of a line between infradentale (ID) and menton (Me): (Sy)[17].

Nearly all growth parameters as calculated from these points are related to bone or tooth implants. Although those markers are placed as accurate as possible in the same regions, they cannot be considered as identical for the different animals. This means that for the description of growth not the distances themselves can be used, but that the increments, i.e. the changes in distances in time have to be considered. The use of increments has also the advantage that in case an implant was replaced, the analysis of the growth could easily be continued.

For analysis of differences in changes of maxillary structures between the two groups relative to the frontal bone implant, increments in vertical and horizontal direction of the distances FB-AU and FB-PU were calculated. A comparable approach was followed for differences in position of the maxillary dentition in relation to maxillary structures by calculating increments of distance PU-TU in vertical and in horizontal direction.

In order to study differences between both groups in mandibular position relative to the frontal bone implant, increments of distances FB-AL and FB-PL were calculated in vertical and horizontal direction. Further increments of the overall length of the mandible (Co-Sy) and the changes in the gonial angle (Me-Go-Co) were determined. To describe changes in position of the mandibular dentition within the mandible, increments of distance TL-PL in vertical and horizontal direction were calculated.

To quantify differences in the jaw relation between both groups and in the position of the mandible in relation to the maxillary dentition, increments in vertical and horizontal direction of the distances PU-AL, PU-PL and TU-PL were calculated.

Differences between the two groups of changes in occlusion were studied by calculating increments of distances TU-TL in horizontal direction. The mean increments of the experimental group were compared with those of the control group using the t-test.

For the interpretation of the findings, the total period under study (29-143 weeks of age) was divided in five sub-periods: an initial one covering the first 10 weeks and four sub-periods of 26 weeks each. The initial period, the four sub-periods, and the main period (consisting of the four sub-periods) were analyzed separately. The data obtained from the initial period showed such a large variation that it was not meaningful to include them in the statistical analysis of the experiment. This large variation was mainly due to difficulties with the positioning of the youngest animals in the cephalostat. Facial growth was analyzed by calculating mean increments in micrometres per week over each period studied.

The total error of the method was determined by measuring 5 sets of independent radiographs from two animals of 86, and two other animals of 110 weeks of age. Between the exposures the animals were removed and replaced in the cephalostat.

The measurement error was studied by double determination of all variables recorded in a longitudinal series of one monkey.

4.4 Results

Error of the method

The total error of the method is composed of the error of the radiographical procedure and the measurement error due to inexact defining of the measuring points, to inaccuracy of the measuring instrument, and the error of the observer. A suitable description of the errors could be obtained by specifying the error in vertical and in horizontal direction, separately for all distances and increments used. In total eight categories of errors were analyzed. Most of the errors were 20 μm or less. Only the errors in the distances and increments in horizontal direction in relation to the frontal bone implant showed comparatively high values of 38 and 60 μm respectively. This error was mainly caused by inaccuracies associated with the determination of the Anterior Cranial Base line.

The total error of the gonial angle was found to be 1.1° and that of the mandibular length 32 μm, which was considered to be acceptable. The measurement error in the increments was calculated as duplicate error and varied for all categories between 12 and 18 μm. The measurement error in the gonial angle showed a value of 0.7°.

Findings

In all considered periods the mean vertical displacement of the maxillary structures relative to the frontal bone implant (FB-AU and FB-PU) was larger in the control group than in the experimental group (Table 4-1). The more the experiment proceeded, the more these differences became obvious, resulting in quite a divergent course of displacement of the maxillary structures for both groups. Significant differences in increments were found for distance FB-AU in the period from 117 to 143 weeks of age and for distance FB-PU from 91 to 143 weeks of age. Over the main period both maxillary bone implants showed smaller mean inferior displacements in the experimental than in the control group, but these differences were only borderline significant.

Table 4-1: *Mean increments (m) and SEM in μm per week of the distances between maxillary bone implants and the frontal bone implant*
** = $p < 0.05$*

Vertical

Age in weeks	FB-AU						FB-PU					
	Control			Exp.			Control			Exp		
	n	m	SEM	n	m	SEM	n	m	SEM	n	m	SEM
29 - 39	7	54	± 11	6	43	± 20	7	68	± 11	6	42	± 11
39 - 65	7	42	± 8	7	32	± 4	7	50	± 8	7	42	± 5
65 - 91	6	31	± 4	6	28	± 5	6	43	± 4	7	35	± 4
91 - 117	6	35	± 8	7	20	± 2	6	43	± 6	7	25	± 3*
117 - 143	6	34	± 3	6	19	± 3*	6	40	± 4	7	24	± 4*
39 - 143	6	35	± 4	6	25	± 3	6	43	± 5	7	32	± 3

Antero-posterior

Age in weeks	FB-AU						FB-PU					
	Control			Exp.			Control			Exp.		
	n	m	SEM	n	m	SEM	n	m	SEM	n	m	SEM
29 - 39	7	102	± 24	6	83	± 8	7	98	± 25	6	84	± 7
39 - 65	7	64	± 7	7	74	± 6	7	62	± 7	7	70	± 6
65 - 91	6	71	± 14	7	62	± 7	6	69	± 5	7	65	± 5
91 - 117	6	45	± 8	7	47	± 4	6	43	± 9	7	48	± 4
117 - 143	6	57	± 8	6	46	± 4	6	55	± 8	7	41	± 8
39 - 143	6	60	± 7	6	57	± 3	6	58	± 7	7	55	± 3

Comparing anterior (FB-AU) and posterior (FB-PU) vertical changes, nearly all posterior vertical increments seemed to be larger than the anterior ones in both groups, although a paired t-test revealed no significant differences for separate periods nor for the main period of the experiment.

The mean increments per week of the antero-posterior displacement of the maxillary structures reduced for all animals when growth proceeded. No difference could be noted between both groups neither for any period nor for the main period of the experiment (Table 4-1).

The mesial migration of the maxillary dentition in relation to the posterior maxillary bone implant, (distance PU-TU) (Table 4-2) was about the same in both groups. This conformity applied to the different periods as well as to the main period of the experiment. Generally, the migration rate decreased with age in all animals.

The inferior displacement of the mandible relative to the frontal bone implant, as measured by the distances FB-AL and FB-PL in vertical direction revealed no significant difference between the two groups (Table 4-3).

Table 4-2: *Mean increments (m) and SEM in μm per week of the distances between the maxillary tooth implant and the posterior maxillary bone implant.*

Antero-posterior

PU-TU

Age in weeks	Control			Experimental		
	n	m	SEM	n	m	SEM
29 - 39	6	59	± 8	5	54	± 11
39 - 65	7	36	± 3	7	37	± 4
65 - 91	6	44	± 3	7	34	± 6
91 - 117	6	21	± 2	7	29	± 4
117 - 143	6	18	± 5	6	18	± 4
39 - 143	6	29	± 1	6	31	± 2

In antero-posterior direction larger anterior displacement of the mandible relative to the implant in the frontal bone (FB-AL, FB-PL) could be suggested for the initial period in the control group than in the experimental group (Table 4-3). Over the main period the anterior displacement of the mandible in the experimental group seemed to be larger than in the control group. However, these differences were not significant, probably due to the large standard errors for measurements in horizontal direction when the frontal bone implant is involved. For both groups the decrease in growth rate and the pattern of displacement were comparable.

Table 4-3: *Mean increments (m) and SEM in µm per week of the distances between mandibular bone implants and the frontal bone implant*

Vertical

Age in weeks	FB-AL Control n	m	SEM	FB-AL Exp n	m	SEM	FB-PL Control n	m	SEM	FB-PL Exp n	m	SEM
29 - 39	7	189	± 24	6	171	± 34	7	221	± 22	6	202	± 36
39 - 65	7	146	± 15	7	154	± 9	7	170	± 17	7	171	± 9
65 - 91	6	101	± 6	7	121	± 12	6	125	± 7	7	133	± 12
91 - 117	6	105	± 10	7	90	± 6	6	110	± 10	7	96	± 6
117 - 143	6	95	± 5	7	80	± 8	6	110	± 6	7	89	± 9
39 - 143	6	110	± 4	7	111	± 6	6	127	± 4	7	122	± 7

Antero-posterior

Age in weeks	FB-AL Control n	m	SEM	FB-AL Exp n	m	SEM	FB-PL Control n	m	SEM	FB-PL Exp n	m	SEM
29 - 39	7	164	± 34	6	141	± 18	7	154	± 32	6	137	± 20
39 - 65	7	99	± 15	7	133	± 6	7	94	± 14	7	127	± 5
65 - 91	6	102	± 15	7	100	± 10	6	100	± 16	7	100	± 1
91 - 117	6	57	± 12	7	71	± 9	6	52	± 11	7	70	± 9
117 - 143	6	72	± 10	7	69	± 5	6	73	± 10	7	69	± 6
39 - 143	6	82	± 8	7	93	± 2	6	80	± 8	7	92	± 2

Table 4-4: *Mean increments (m) and SEM in µm per week of the mandibular length, mean increments (m) and SEM in degrees per week of the gonial angle, mean increments (m) and SEM in µm per week of the distance between the mandibular tooth implant and the mandibular posterior bone implant, Negative changes indicate a closure of the gonial angle or a decrease in a distance * = p < 0 05*

Antero-posterior
Co-Sy

Age in weeks	Control			Exp		
	n	m	SEM	n	m	SEM
29 - 39	7	250	± 20	6	264	± 42
39 - 65	7	200	± 19	7	207	± 15
65 - 91	6	150	± 10	7	175	± 11
91 - 117	6	154	± 10	7	140	± 7
117 143	6	140	± 18	7	117	± 14
39 143	6	160	± 9	7	160	± 5

Me Go Co

Age in weeks	Control			Exp		
	n	m	SEM	n	m	SEM
29 - 39	7	-1 14	± 1 74	6	0 92	± 1 64
39 - 65	7	-0 70	± 0 26	7	-0 74	± 0 45
65 - 91	6	-0 57	± 0 29	7	0 38	± 0 16*
91 - 117	6	0 68	± 0 28	7	0 05	± 0 32
117 - 143	6	0 48	± 0 32	7	-0 36	± 0 21
39 - 143	6	-0 06	± 0 14	7	-0 17	± 0 13

TL PL

Age in weeks	Control			Exp		
	n	m	SEM	n	m	SEM
29 39	6	- 9	± 10	7	12	± 8
39 - 65	7	-10	± 6	7	4	± 4
65 - 91	6	-13	± 4	7	-12	± 4
91 117	6	- 9	± 4	7	1	± 2
117 - 143	6	9	± 7	7	9	± 4
39 143	6	- 6	± 3	7	0	± 2

Table 4-5: *Mean increments (m) and SEM in μm per week of the distances between the maxillary bone implants or the maxillary dental implant, and the mandibular bone implant; Negative changes indicate a decrease in a distance.* * = $0.01 \leq p < 0.05$; ** = $p < 0.01$.

Vertical

Age in weeks	PU-AL Control n	m	SEM	PU-AL Exp. n	m	SEM	PU-PL Control n	m	SEM	PU-PL Exp. n	m	SEM
29 - 39	7	120	± 21	6	129	± 25	7	152	± 21	6	159	± 27
39 - 65	7	95	± 8	7	112	± 7	7	120	± 10	7	129	± 7
65 - 91	6	58	± 7	7	86	± 9*	6	83	± 6	7	97	± 10
91 - 117	6	62	± 5	7	65	± 4	6	67	± 4	7	71	± 5
117 - 143	6	56	± 5	6	57	± 7	6	70	± 3	6	66	± 8
39 - 143	6	66	± 1	6	81	± 5*	6	84	± 2	6	93	± 5

Antero-posterior

Age in weeks	PU-AL Control n	m	SEM	PU-AL Exp. n	m	SEM	PU-PL Control n	m	SEM	PU-PL Exp. n	m	SEM
29 - 39	7	66	± 11	6	57	± 13	7	56	± 8	6	52	± 15
39 - 65	7	37	± 9	7	63	± 7*	7	32	± 9	7	57	± 6*
65 - 91	6	33	± 6	7	36	± 6	6	31	± 6	7	36	± 6
91 - 117	6	14	± 3	7	23	± 5	6	8	± 4	7	23	± 6
117 - 143	6	17	± 4	6	27	± 5	6	18	± 4	6	28	± 6
39 - 143	6	25	± 3	6	39	± 3*	6	22	± 2	6	37	± 3**

Age in weeks	TU-PL Control n	m	SEM	TU-PL Exp. n	m	SEM
29 - 39	6	3	± 15	5	-3	± 19
39 - 65	7	4	± 7	7	-20	± 6*
65 - 91	6	12	± 5	7	-2	± 7
91 - 117	6	12	± 3	7	6	± 6
117 - 143	6	0	± 5	7	-6	± 5
39 - 143	6	8	± 3	7	-6	± 3**

The length of the mandible, as represented by distance Co-Sy also showed a continuously decreasing growth rate throughout the experimental period and seemed not to be affected by the elimination of interdigitation. That also applies to the gonial angle (Me-Go-Co) for which no significant differences were found except from 65 to 91 weeks of age. None of the recordings of the mandibular dentition within the mandible, as measured by variable TL-PL, in the antero-posterior direction showed any significant differences between both groups (Table 4-4).

The increase in the distances in vertical direction between the maxillary and the mandibular bone implants (PU-AL) and (PU-PL) tended to be larger in the experimental than in the control group in almost every period. However, significant differences were only found for variable PU-AL from 65 to 91 weeks of age and for the main period of the experiment. For distance PU-PL no significant differences between the groups were found for any of the periods (Table 4-5).

In the experimental as well as in the control group, the mandible moves more anteriorly than the maxilla. This difference is significantly more pronounced in the experimental than in the control group if the main period is considered (Table 4-5).

As could be expected from the data in Table 4-2 and 4-5, the maxillary dentition in the control group moved more in anterior direction than did the mandibular bone (TU-PL > 0). In the experimental group on the contrary, the maxillary dentition moved less anteriorly than the mandible (TU-PL < 0). This results in significant differences between the groups for the period from 39-65 weeks of age and for the main period (Table 4-5).

Distance TU-TL in antero-posterior direction is a measure for the occlusion. This distance showed a significant larger increment for the experimental group than for the control group over the main period of the experiment indicating the development of a more mesio-occlusion in the experimental group (Table 4-6).

Table 4-6: *Mean increments (m) and SEM in micrometers per week of the distances between the tooth implants. Negative changes indicate a decrease in distance.*
** = p < 0.05.*

Antero-posterior

TU-TL

Age in weeks	control			experimental		
	n	m	SEM	n	m	SEM
29 - 39	6	0	± 10	5	20	± 18
39 - 65	7	6	± 3	7	17	± 6
65 - 91	6	0	± 2	7	13	± 6
91 - 117	6	-4	± 3	7	-5	± 5
117 - 143	6	-9	± 10	7	0	± 3
39 - 143	6	-1	± 2	7	6	± 2*

4.5 Discussion

The role of the interdigitation in the sagittal development of the maxillo-mandibular complex was studied in an experimental set-up without surgical intervention, growth restriction or stimulation. Skeletal as well as dental parameters were used for the analysis.

Findings from this longitudinal study indicate that elimination of the interdigitation results in a deviating maxillo-mandibular development.

The development of the maxillary structures in vertical direction was reduced by the elimination of the interdigitation. This inhibition became more pronounced as the follow-up advanced. At the posterior region the reduction became significant at week 91, and at the anterior region from week 117 on. Since the differences between the control and the experimental group only became significant more than 65 weeks after the start of the experiment, the grinding of the cusps of the teeth itself could not be held responsible for this effect. Although a quite divergent course in vertical development at the maxillary structures of both groups existed, no significant inhibition of development was found for the total experimental period. This might be due to relative large individual variation at the start of the experiment.

Since the establishment of the initial occlusal contact of the first permanent molars more or less coincides with the start of a significant decrease in vertical development of the posterior part of the maxillary structures, the experimental findings seems to confirm the assumption of Moyers and Wainright[3] that the occlusion of these teeth influences the naso-maxillary and alveolar growth.

In the experimental animals the smaller increase in vertical development of the maxillary structures at the end of the experimental period coincides with a larger increase in height at the maxillary and mandibular alveolar process, resulting in a seemingly unaffected development of the vertical facial height.

As described elsewhere, the palatal plane in the young and adolescent untreated *Macaca fascicularis* tends to tilt in counter-clock-wise direction during growth[18,19]. The palatal plane of the experimental group seemed to undergo an accentuated tilting as compared to the control group, because the vertical growth reduction at the anterior part of the maxillary structures was slightly larger than at the posterior part.

In antero-posterior direction, the development of the maxillary structures in the experimental group seemed to be unaffected. The same applies to the morphology of the mandible, as represented by its total length and gonial angle. As the mandible attained a significantly more anterior position in relation to the maxilla. This indicates that adaptations necessary for proper functioning of the temporo-mandibular joint probably take place at the glenoid fossa, which is in accordance with the findings of Hinton and McNamara[20] in M. mulatta. The final outcome is that a more prognathic face developed in the experimental than in the control group.

It can be concluded that interdigitation is an important factor in the control of the antero-posterior relationship between the jaws and as such supports the ideas of Brace[1], Van der Linden[2], Nanda *et al.*[4,5], and Sarnat[9,10]. That also applies to the cybernetic model of Petrovic *et al.*[6,7,8] in which is assumed that the occlusion is the basis for the adjustment of the relationship between the jaws. It further suggests, that if occlusion is eliminated, the correlation in antero-posterior growth between the jaws is lost.

The fact that morphology and size of the mandible did not seem to adapt to its deviating position, might indicate that its growth is more or less independent of the interdigitation. The more prognathic facial development in the experimental groups resulted in a more mesial occlusion as the mandibular molars did not show signs of mesiodistal migration in relation to the mandibular basal structure.

It is most likely that in the untreated *Macaca fascicularis* the adjustment of the antero-posterior growth between the jaws is mainly realized by positional adaptation of the mandible and of the mandibular posterior teeth.

4.6 Conclusions

This experiment on juvenile *Macaca fascicularis* on the role of the interdigitation in the development of the maxillo-mandibular complex leads to the following conclusions:

1. Interdigitation plays a role in the vertical development of the maxillary structures but seems not to influence their antero-posterior development.
2. Interdigitation plays a role in the antero-posterior positioning of the mandible, but seems not to affect its growth.
3. Elimination of interdigitation results in a skeletal Class III pattern. Lack of distal migration of the posterior teeth through the mandibular basal structures, leads indirectly to mesio-occlusion.
4. Under normal conditions interdigitation contributes to growth and development of the maxillo-mandibular complex in *Macaca fascicularis*.

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Chapter 5

The role of the intercuspation in the regulation of transverse maxillary development in *Macaca fascicularis*

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5.1 Summary

The role of the intercuspation of the teeth in transverse maxillary growth and dental arch development was investigated radiographically with the aid of implants in *Macaca fascicularis* monkeys. Fourteen animals were randomly allocated to a control group (n = 7) and an experimental group (n = 7) and were followed from 29 to 100 weeks of age.

Intercuspation was eliminated in the experimental group by grinding the canine and molar cusps in both dental arches as soon as possible after emergence. Maxillary occlusal radiographs were taken at regular intervals. Linear and angular analysis of skeletal changes revealed that mid-palatal sutural growth seems to be independent of intercuspation. The developing dental arch, however, showed a significantly greater increase in width in certain areas in the experimental group than in the control group. Most findings support the hypothesis that the width of the maxillary dental arch is guided by the width of the mandible through the intercuspation of the posterior teeth.

5.2 Introduction

Normal dento-facial growth and development strongly suggest a coordination in the development of the dentition of both jaws. The occlusal anatomy of the posterior teeth or, more specifically, their intercuspation is supposed to play a major role in this process. The cone shaped cusps of the maxillary posterior teeth and the crater-like occlusal anatomy of their antagonists are responsible for a guided emergence towards each other, by the so-called cone-funnel mechanism[1,2], leading to the final occlusion. This coordination mechanism might extend its influence beyond the dentition, as hypothesized by Brace[3]. He proposed that intercuspal relationships may act as a guidance system for the growth of bony structures in the developing face.

In 1986 Van der Linden[4] developed a more detailed hypothesis, stating that once occlusal contact is established, further transverse development of the maxillary dental arch and its surrounding maxillary structures is regulated by the mandibular dentition via intercuspation. The mandibular dental arch would function as a rail guiding the development of the maxillary arch. In instances where normal vertical contact is lacking in the posterior region (posterior open bite) the transverse development of the maxillary dental arch is disturbed. In those cases the rail mechanism cannot be effective, resulting in a narrow maxillary arch in most cases[4].

Zingeser[5] presented an opposite view when he theorized that the mandible and its dentition accommodate to a so-called upper occluso-facial functional component, which implicates the guidance of mandibular growth by the maxilla.

Sarnat[6,7] presented experimental evidence showing that the occlusion contributes to a harmonious intermaxillary relationship. He resected the median and transverse palatine sutures in *Macaca mulatta* and studied jaw growth thereafter. He found that the surgery did not significantly influence maxillary growth and he concluded that the mandible might guide the growth of the maxilla by means of occlusion and intercuspation.

In an extensive series of experiments in rats, Petrovic and co-workers[8,9,10], influenced growth of the maxillo-facial complex in rats by a variety of interventions, including different orthopaedic devices, sectioning of the lateral pterygoid muscle, tongue reduction, and the administration of growth hormones. Their experiments resulted in a hypothetical servo-system in which they suggest the importance of a peripheral comparator for the coordination of the growth of the upper and lower jaws and for the maintenance of an optimal occlusal relationship.

On the other hand, Kantomaa and Rönning[11], also using rats, restricted maxillary growth by creating synostoses of maxillo-facial sutures, with or without elimination of intercuspation. In both situations they found that the inhibition of maxillary growth was accompanied by a slowing down of mandibular growth. As the effects appeared to be independent of intercuspation, they concluded, in contrast to Petrovic *et al.*, that intercuspation does not seem to play a role in the coordination of mandibular and maxillary growth.

A drawback of all these experimental studies is that dento-facial development has been impaired surgically or by orthopaedic devices. These may hamper extrapolation of the findings to normal growing human systems, due to possible iatrogenic effects or due to marked differences in morphology and physiology of the maxillo-facial complex between rodents and humans. Data derived from experiments on non-human primates might yield more relevant information[12,13,14,15].

In particular, growth and development of the maxillo-facial complex of members of the *Macaca species* show basic similarities to humans[15,16,17]. *Macaca* and humans have the same number of deciduous and permanent teeth, a comparable dental morphology, posterior occlusion, and intercuspation, although all dimensions are smaller in *Macaca*. Also the development of the dentition, including tooth eruption and the sequence of transition, is highly comparable in *Macaca* and humans[15,16,17].

The purpose of this study, therefore, was to investigate the contribution of intercuspation to the transverse development of the maxilla and its dental arch in an experimental model in which intercuspation was eliminated but growth was not otherwise disturbed.

5.3 Materials and methods

Experimental procedures

Eleven male and three female laboratory-born monkeys (*Macaca fascicularis*) were used in this study. All animals showed a neutro-occlusion of the posterior teeth and an occlusion in the frontal region between a nearly end-to-end and a light overjet and overbite. None of the animals had a malocclusion or a skeletal deviation. The mean age of the animals was 29 weeks at the start of the study. At that stage, crypt formation of the mandibular permanent canines had become visible radiographically and the second deciduous molars had recently emerged[18]. The study lasted until the animals were 100 weeks of age, which is after occlusal contact of the first permanent molars was established.

The animals were randomly allocated to a control group (n = 7) and an experimental group (n = 7). The groups were balanced for dental development, dental arch dimensions, and age. One male animal of the control group died accidentally after one year. All animals were housed in the Central Animal Laboratory of the University of Nijmegen, the Netherlands, and received a standard diet of wet compressed pellets and drinking water *ad libitum*.

At the start of the study 4 tantalum implants (Ole Dich, Hvidovre, Denmark), measuring 1.2 mm in length and 0.5 mm in width, were inserted as bone markers in each monkey[19,20]. The animals were premedicated with 10 mg/kg Ketamine (Nimatek^R, A.U.V., Cuijk, The Netherlands) then brought under general anaesthesia with 0.1 ml Thalamonal^R (Janssen Pharmaceutica, Beerse, Belgium) and 0.25 mg Atropine (Atropine Sulphate 0.5 mg/ml, A.C.F. Pharma B.V., Maarssen, The Netherlands). One pair of implants were inserted into the palate through the mucosa at each side of the mid-palatal suture and checked for stability (Fig. 5-1).

As soon as possible after emergence, the deciduous and permanent molars in both groups were provided with tantalum balls with a diameter of 0.5 mm. The animals were then brought under general anaesthesia, and a small hole was prepared with a round bur in the buccal surface of each molar in which the implant was secured with composite material. If a radiograph showed that a bone or tooth implant had become loose, a new one was immediately inserted as close as possible to the position of the loose one, and the radiographic procedure was repeated.

In the animals of the experimental group, the intercuspation was eliminated by grinding the cusps of the deciduous molars and canines and the first permanent molars so that flat surfaces were obtained in both dental arches. The grinding was performed under general anaesthesia as soon as possible after emergence of the cusps. The cusps were ground without jeopardizing the vitality of the pulp. The proximal contacts of the deciduous and permanent molars were not involved in the grinding.

In both groups standardized occlusal radiographs of the maxilla were taken with the aid of a cephalostat. Initially this was done every three weeks, but after the maxillary first permanent molars had attained the level of the occlusal plane, the frequency was reduced to once every six weeks. The animals were brought under general anaesthesia prior to fixation in the cephalostat. The radiographic films were attached to a film carrier to prevent bending and placed into the mouth touching the maxillary teeth. The central beam of the X-ray machine was orientated perpendicular to the occlusal plane and the radiographic film. The distance between the X-ray focus and the occlusal plane was fixed at 4.5 m. The radiographs were made with 100 kV at 20 mA and 5 seconds exposure time. After the maxillary permanent first molars had reached the level of the occlusal plane, the exposure time was increased to 7.5 seconds.

Both sexes were combined in the analysis of the data, as sexual differences in craniofacial growth and development in *Macaca fascicularis* become apparent only after the age of three years, and therefore can be neglected for the purpose of this study[21].

Measurements (radiographic analysis)

The coordinates of the bone and tooth implants on the occlusal radiographs were digitized with the Optocom measuring instrument[22]. All recordings were performed by the first author. To quantify dental arch dimensions and their changes over time on the radiographs, a Cartesian coordinate system was constructed with the best fit line through the central incisor point and three points at the centre of the mid-palatal suture as Y-axis and a perpendicular through the central incisor point as X-axis (Fig. 5-1).

In this coordinate system the following measuring points were used to study the transverse maxillary growth and dental arch development (Fig. 5-1):

1. right anterior palatal bone implant (RAB)
2. right posterior palatal bone implant (RPB)
3. left anterior palatal bone implant (LAB)
4. left posterior palatal bone implant (LPB)
5. right first deciduous molar implant (RFD)
6. right second deciduous molar implant (RSD)
7. right first permanent molar implant (RFP)
8. left first deciduous molar implant (LFD)
9. left second deciduous molar implant (LSD)
10. left first permanent molar implant (LFP)

Measurement error was estimated by measuring all radiographs of one monkey twice with an interval of two weeks. The error of the radiographic procedure was determined using the radiographs of two animals at the start and two at the end of the experimental period. For each monkey the radiographic procedure was repeated five times, removing and replacing the animal in the cephalostat each time.

Changes in dental arch width dimensions were studied by calculating the increments of following distances, parallel to the X-axis: RFD-LFD, RSD-LSD, and RFP-LFP.

Skeletal changes were analyzed in the same coordinate system. Linear data were obtained by calculating the increments of the transverse distances parallel to the X-axis between the anterior (RAB-LAB) and between the posterior bone implants (RPB-LPB). An angular analysis was applied to detect a possible rotation of the two sides of the palate by calculating the changes in the angle between the lines through the left (LAB-LPB) and right (RAB-RPB) bone implants (Fig. 5-1).

Although the markers were placed as accurate as possible in the same region, they could not be considered identical for the different animals. This means that for a description of growth, the distances themselves cannot be used, and the increments must be considered. The use of increments has also the advantage that, in case an implant was replaced, the analysis of growth could easily be continued using the new marker.

Statistical procedures

Prior to statistical analysis, the symmetry of the jaws was statistically evaluated by the "symmetry analysis" as described in the Appendix.

For statistical analysis of dental arch dimensions and linear skeletal parameters, the experimental period was divided into a first period, which lasted from the start at 29 weeks of age until 75 weeks of age (before the first permanent molar could be used in the measurements), and a second period, which lasted from 75 weeks until 100 weeks of age.

Changes in distances between tooth implants in the X-direction for each period were calculated as mean increments and their standard errors in μm per week.

To compensate for size differences among the animals, an analysis of co-variance was performed on the distances between the tooth implants of the first deciduous molars of each monkey at 30 weeks of age. The Student's t-test was used to analyze differences between the control group and the experimental group, and a paired t-test was used within the groups to detect differences between the two periods.

Changes in distances between skeletal implants in the X-direction over each period were calculated as mean increments and standard errors in μm per week.

The situation is complicated by a possible rotation of the two sides of the palate. This means that the local amount of sutural growth might be partly dependent on the position of the bone marker along the length of the suture. To cope with this problem, the initial mid-sagittal positions for both the anterior and the posterior bone implants for each animal were calculated (see Fig. 5-1: m and m'). Since these initial mid-sagittal positions of the anterior and posterior bone implants differed among individuals, an analysis of co-variance was carried out. Compensation for size differences was also carried out by analysis of co-variance.

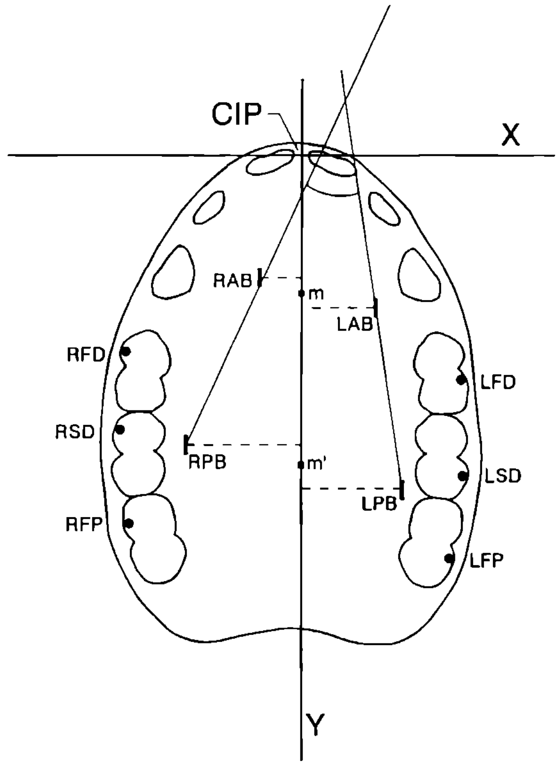

Figure 5-1: *Schematic drawing of the palate and the dentition after emergence of the first permanent molars, showing the coordinate system and the positions of the bone and tooth implants. Initial mid-sagittal position for anterior and posterior bone implants are indicated as m and m' respectively. For the angular analyses the changes in the angle between the lines connecting the left and the right bone implants were calculated.*

Differences between the groups were analyzed using Student's t-test and within the groups using the paired t-test.

For the analysis of the angular measurements, the experimental period was considered as a whole. Mean changes were calculated in degrees/week. Two animals from the experimental group were excluded from this part of the study as their bone implants at one of the palatal halves were too close together to obtain accurate angle measurements. The t-test was used for analysis of the differences between the control and the experimental groups.

5.4 Results

The results are summarized in Table 5-1. Significant differences are indicated by superscript characters to which is referred in the text.

Error of the method

The total error of the method is made up of the errors of the radiographic procedure and the measurement.

The measurement error of the occlusal radiographs was found to be about 50 μm for the distances. The error of the radiographic procedure was found to be about 60 μm for the distances, resulting in a total error of the method of about 80 μm, which was considered to be acceptable.

Dental arch width changes

In the control group no significant differences between the two periods were found for the mean increments of the distances between the first and the second deciduous molars (RFD-LFD and RSD-LSD). In the experimental group the increase of the distance between the first deciduous molars (RFD-LFD) was significantly larger in the first than in the second period ($0.01 \leq p < 0.05$, [A]), but such a difference could not be found for the second deciduous molar width (RSD-LSD).

No differences were found between the experimental and the control groups in the first period for any of the changes in arch width dimensions. In the second period the increase in the distance between the second deciduous

Table 5-1: *Dental arch width changes and transverse linear skeletal changes: mean increments ± SEM in μm per week of the transverse distances between the tooth implants (RFD-LFD, RSD-LSD, RFP-LFP) and between the maxillary anterior (RAB-LAB) and posterior (RPB-LPB) bone implants. n per group varying from 4 to 7.*

Anterior region				
Age in weeks	Control		Exp.	
	Dent.	Skel.	Dent.	Skel.
	RFD-LFD	RAB-LAB	RFD-LFD	RAB-LAB
29 - 75	46 ± 4	36 ± 5^{D}	$49 \pm 4^{A,H}$	$32 \pm 3^{G,H}$
75 - 100	26 ± 5	31 ± 1^{E}	28 ± 2^{A}	31 ± 1^{F}

Posterior region				
Age in weeks	Control		Exp.	
	Dent.	Skel.	Dent.	Skel.
	RSD-LSD	RPB-LPB	RSD-LSD	RPB-LPB
29 - 75	41 ± 7	53 ± 7^{D}	38 ± 8	47 ± 4^{G}
75 - 100	$32 \pm 4^{B,J}$	$44 \pm 4^{E,J}$	44 ± 3^{B}	45 ± 2^{F}

Posterior region				
Age in weeks	Control		Exp.	
	Dent.	Skel.	Dent.	Skel.
	RFP-LFP	RPB-LPB	RFP-LFP	RPB-LPB
75 - 100	27 ± 4^{C}	44 ± 4	38 ± 3^{C}	45 ± 2

molars (RSD-LSD) was significantly larger in the experimental group than in the control ($0.01 \leq p < 0.05$, [B]). Also, the distance between the first permanent molars (RFP-LFP) tended to increase more in the experimental group ($0.05 \leq p < 0.1$, [C]). However, such a trend did not occur for the distance between the first deciduous molars (RFD-LFD).

Transverse linear skeletal changes

Neither the control nor the experimental group, showed significant differences in the rate of sutural growth between the two periods. This applies for the anterior as well as for the posterior regions (RAB-LAB and RPB-LPB).

The increase of the distance between the posterior implants (RPB-LPB) tended to be larger than that between the anterior implants (RAB-LAB) in both groups and in both periods ($0.05 \leq p < 0.1$, [D,E,F]). However, the only significant difference was found in the experimental group, where in the first period the posterior bone markers (RPB-LPB) diverged significantly more than the anterior ones (RAB-LAB; $p < 0.01$, [G]).

Dental arch width changes versus transverse linear skeletal changes

The increments of dental and skeletal dimensions were of the same order of magnitude, indicating an important contribution of sutural growth activity in the widening of the dental arch. However, in the first period a significant buccal drift of the first deciduous molars (RFD-LFD > RAB-LAB) occurred in the experimental group ($0.01 \leq p < 0.05$, [H]). Such a drift could not be detected in the control group.

In the second period, all deciduous and first permanent molars in the experimental group seemed to undergo only a passive buccal displacement, while in the control group the second deciduous molars showed significant less lateral displacement than the corresponding bone implants (RSD-LSD > RPB-LPB; $p < 0.01$, [J]). Comparison of the lateral displacement of the first permanent molars with that of the bone implants only suggests a phenomenon comparable to that found for the second deciduous molar area.

Angular skeletal changes
The angular changes were limited. In the control group the mean increase of the angle between the lines RAB-RPB and LAB-LPB amounted 0.11 ± 0.01° per week, in the experimental group the mean increase was 0.15 ± 0.02° per week. Student's t-test revealed no significant differences between the groups, but both values were significant differing from zero ($p < 0.01$).

5.5 Discussion

Animal experiments on the role of intercuspation in the regulation of dental arch width increase and transverse maxillary growth involve surgical intervention or mechanical influence by orthopaedic appliances[6-11]. This limits the reliability of extrapolating the findings to normal growing individuals. In the present study iatrogenic growth disturbances were avoided and *Macaca fascicularis* was used, as data obtained from occlusal research in this species are particularly suited for extrapolation to the human situation[12-17].

The current study demonstrated that mid-palatal sutural growth in *Macaca fascicularis* occurs at a faster rate posteriorly than anteriorly, leading to rotation of the maxillary halves. This observation is in agreement with the findings of Björk and Skieller[23] who called this phenomenon, when they observed it in humans, "Transverse Mutual Rotation". No significant differences in transverse maxillary skeletal growth were found between the experimental and control groups, indicating that neither sutural growth nor the "Transverse Mutual Rotation" controlled by intercuspation. This contradicts the concept of the rail mechanism as suggested by Van der Linden[4], which also assumes an effect of intercuspation on maxillary sutural growth.

In the first period no differences in increase of dental arch width between the control and the experimental animals was found. In the second period the dental arch width of the deciduous second molars and the first permanent molars increased faster in the experimental group than in the control animals.

If the skeletal and the corresponding dental data are combined, differences between the groups become more apparent. In the first period the deciduous first and second molars in the control group seem to move passively with the bone. In the experimental group, however, buccal movement of the deciduous first molar is significantly faster than that of the bone. In the second period the deciduous molars and the permanent first molars seem to move passively in the experimental animals, while in the control animals the buccal movements of the second deciduous molars and the first permanent molars are slower than the bone.

This means that in monkeys in which intercuspation was eliminated, the maxillary dental arch width increased relatively more than in animals with a normal intercuspation.

These findings do not fit the concept of Kantomaa and Rönning[11] who state that the maxilla acts as a carrier for mandibular growth in sagittal direction, or the idea of Zingeser[5] that the maxilla serves as a template to which mandibular growth adapts.

Our findings are in agreement with the concept of Sarnat[6,7], which states that, in monkeys, intercuspation plays a guidance role in maxillary dental arch development. Our findings also support the idea of some sort of rail mechanism, but in contrast to the concept of Van der Linden[4], which assumes a stimulation of transverse growth of the maxillary dentition by the growing mandible, intercuspation in monkeys seems to act as a restraining factor.

For a proper interpretation of the data spatial relationships between the jaws must be considered. In juvenile monkeys, unlike in humans, the base of the maxillary structures is wider than the base of the mandibular structures in the premolar and molar region, as revealed by CT-scans (unpublished data). An adjustment of dental arch width dimension of the two jaws in humans requires a widening of the maxillary arch and thus a propulsive action of the mandibular dentition, while in monkeys the maxillary dentition has to adapt to a narrow mandibular dental arch. A further indication that this indeed might be the case is found in the inclination of the posterior teeth. In humans the mandibular posterior teeth are lingually inclined and the maxillary ones buccally inclined, while in monkeys a reversed inclination of the posterior teeth is found.

The findings of our study suggest that the concept of Van der Linden[4] must be modified: the transverse development of the maxillary dental arch seems to be guided in a stimulating or restraining way by the mandibular arch by means of the intercuspation of the posterior teeth. The ratio of the transverse growth capacities of both jaws might determine the trend of the interaction.

Another necessary modification in the rail mechanism hypothesis might be that the coordinating role is restricted to the development of the dental arch and that midpalatal sutural growth is not involved.

5.6 Conclusions

This experiment in *M. fascicularis* on the role of intercuspation in the transverse maxillary development leads to the following conclusions:

1. Intercuspation is likely most responsible for guiding the teeth into their occlusal relationships with the opposing arch.
2. Intercuspation does not contribute to the transverse growth and development of the maxillary bone in *M. fascicularis*.

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Chapter 6

Contribution of the interdigitation to the occlusal development of the dentition in *Macaca fascicularis*

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6.1 Summary

The contribution of interdigitation to the development of the dentition of juvenile *Macaca fascicularis* was studied on series of dental casts and at the histological level by the use of vital staining. Fourteen laboratory-born monkeys were allocated to a control group (n = 7) or an experimental group (n = 7). They were followed from 31 to 152 weeks of age. In the animals of the experimental group interdigitation was eliminated by gradually grinding the cusps of the molars and canines in both dental arches as soon as possible after emergence.

Silicone impressions of the dental arches of each monkey were taken at regular intervals. Two experimental and two control animals received vital stains at regular intervals and were processed for histological evaluation at the end of the experimental period.

Changes over time in the dimensions of the dentition were analyzed. Locally, the maxillary dental arch in the experimental group broadened significantly faster than in the control group. No significant differences between the experimental and the control group were found for any of the mandibular parameters.

The experimental intervention led also to less prevalence of anterior open bite in the experimental group than in the control group.

It is concluded that the interdigitation plays a role in the development of the maxillary dental arch and does not seem to affect mandibular dental arch development.

6.2 Introduction

Interdigitation probably plays a role in the coordination of the development of the mandibular and maxillary dental arches (Schwartz, 1951; Van der Linden, 1983). The cone-shaped cusps of the maxillary posterior teeth and the crater-like occlusal anatomy of their antagonists are held responsible for a guided emergence toward each other by the so-called cone-funnel mechanism (Schwartz, 1951).

Possibly, this mechanism exerts its influence also beyond the dentition, as was hypothesized by Brace (1977). He supposed that intercuspal relationships act as a guidance system for the developing face. This is in agreement with Petrovic and co-workers (Petrovic *et al.*, 1975; Stutzmann and Petrovic, 1976; Petrovic and Stutzmann, 1977) who concluded from a series of experiments in rats that occlusion is an important factor in the coordination of jaw growth, in contradiction to Kantomaa and Rönning (1985) who did not find any evidence for such a regulation system.

Van der Linden in 1986 developed a more elaborate hypothesis stating that once occlusal contact is established, further transverse development of the maxillary dental arch and its surrounding maxillary structures is regulated by the mandibular dentition by means of interdigitation. Due to the rigidity of the mandibular basal anatomy and the already mineralized symphysis, the mandibular dental arch would function as a mould or a rail to which the maxillary dental arch would adapt. By this so-called rail-mechanism normal inter-arch relations are maintained under varying skeletal relationships by the "dento-alveolar compensatory mechanism" (Solow, 1980). Consequently, elimination of interdigitation would result in a disturbance in the development of the maxillary arch but it would not affect mandibular dental arch development.

An opposite view was expressed by Zingeser (1973), who stated that facial capsules are the determinants for facial configuration and hence for the gross orientation in the maxillary dento-alveolar region. The more accurate orientation is, in his opinion, mediated by neuro-muscular mechanisms. In his concept the mandible and its dentition will accommodate to a so-called upper occluso-facial component which implies guidance of the mandibular growth and dento-alveolar development by the maxilla. This would mean that elimination of interdigitation results in a disturbance of the development of the mandibular dental arch and in a normal maxillary development.

All experimental studies on this subject (Petrovic *et al.*, 1975; Stutzmann and Petrovic, 1976; Petrovic and Stutzmann, 1977; Kantomaa and Rönning, 1985) deal with interference of the dento-facial development by surgical interventions or orthopaedic devices in animal models with a normal interdigitation. The present study was designed the other way round, with the purpose of investigating the contribution of interdigitation to maxillary and mandibular dental arch development in growing *Macaca fascicularis* monkeys by only eliminating interdigitation. The effects of this intervention were studied by measurements on a series of dental casts and histological evaluation.

6.3 Materials and methods

Experimental set-up

Eleven male and three female laboratory-born crab-eating monkeys (*Macaca fascicularis*) were assigned to a control group (n = 7) and an experimental group (n = 7), after balancing for dental development, dental arch dimensions, and age. The sexes were combined in the analysis of the data, as sexual differences in *Macaca fascicularis* are found only after three years of age (Swindler and Sirianni, 1973), which is beyond the scope of this study. One male monkey of the control group died accidentally after one year.

All selected animals had a neutro-occlusion of the posterior teeth and a nearly end-to-end occlusion in the anterior region. None of the animals had a malocclusion or a skeletal deviation. At the start of the study, the mean age of the animals was 31 weeks. At that age crypt formation of the mandibular permanent canines had started and the second deciduous molars had recently emerged (Ostyn *et al.*, 1995a). The study lasted until 153 weeks of age.

Figure 6-1 shows the sequence of emergence of the teeth during the experimental period. These data are partly based on Ostyn *et al.* (1995a) and partly on Bowen and Koch (1970).

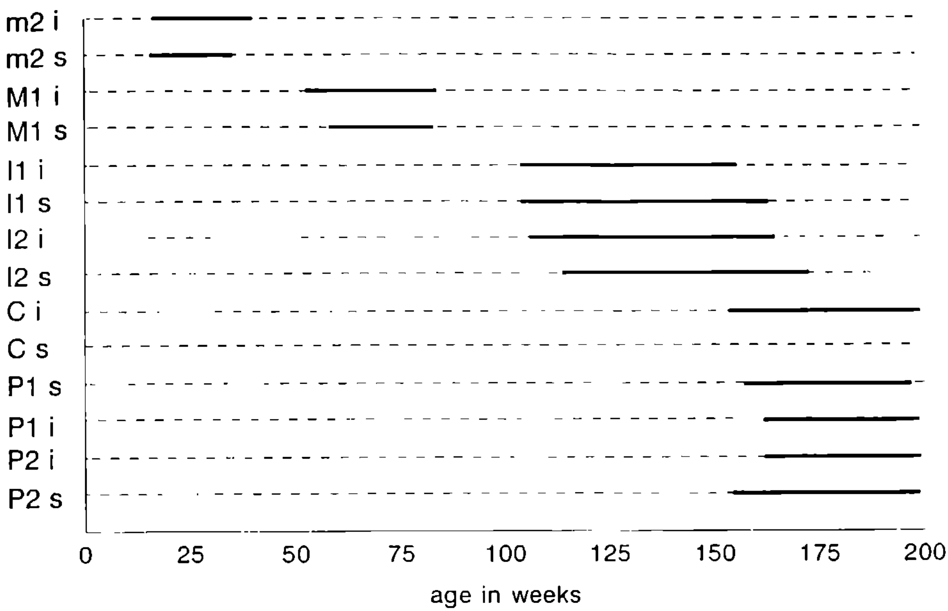


Figure 6-1: *Graphic presentation of ages (ranges) of emergence of teeth between 25 and 200 weeks of age.*

The animals were housed in the Central Animal Laboratory of the University of Nijmegen, The Netherlands, and they received a standard diet of wet compressed pellets and drinking water *ad libitum*.

Anaesthesia

Prior to all experimental interventions or the taking of impressions of the dentition, the animals were premedicated with 10 mg/kg Ketamine (Nimatek^R, A.U.V., Cuijk, The Netherlands). Subsequently, general anaesthesia was produced by 0.1 ml Thalamonal^R (Janssen Pharmaceutica, Beerse, Belgium) and 0.25 mg Atropine (Atropine Sulphate, A.C.F. Pharma B.V., Maarssen, The Netherlands) intramuscularly.

Experimental intervention

In the animals of the experimental group interdigitation was eliminated in several subsequent sessions by gradually grinding the cusps of the deciduous molars, first permanent molars and the deciduous canine tips in both dental arches as soon as possible after emergence until a flat surface was obtained. The grinding did not affect the approximal contact points. The canine cusps were ground as much as possible without jeopardizing the vitality of the pulp.

Dental casts and measurements

Silicone impressions (Xantopren^R, Bayer, Leverkusen, Germany) of the jaws were taken every three weeks during the first part of the study. Once the maxillary first molars had reached the occlusal plane, impressions were taken every six weeks. Impressions were poured out the same day as they were taken.

Measurements on the dental casts were performed using an Optocom measuring table, equipped with a microscope, resulting in a ten times magnification (Van der Linden *et al.*, 1972). Each dental cast was orientated in a Cartesian coordinate system with the Y-axis as a line through the central incisor point (CIP = midpoint between the mesial anatomical contact points of the central incisors) and the middle of the two distal most measuring points at the right and left side of the dental arch, and the X-axis as a perpendicular to the Y-axis through CIP. The position of each tooth was digitized as the midpoint between the anatomical contact points. Where a diastema existed, these points were defined as the most mesial and most distal points of a tooth (Fig. 6-2). All measurements were performed by the same observer (I.H.). For the determination of the total error of the method the dental casts of one younger and one older monkey were measured twice.

To study transverse development of the dental arches in both jaws, increments of the following distances between the posterior teeth were calculated parallel to the X-axis and recorded in μm/week: the distance between the deciduous canines (c-c), the distances between the deciduous first and second molars (m_1-m_1 and m_2-m_2), and the distance between the permanent first molars (M_1-M_1) (Fig. 6-2). To analyze the differences in the transverse development of the jaws, the increments of corresponding transverse maxillary and mandibular dental arch dimensions were compared.

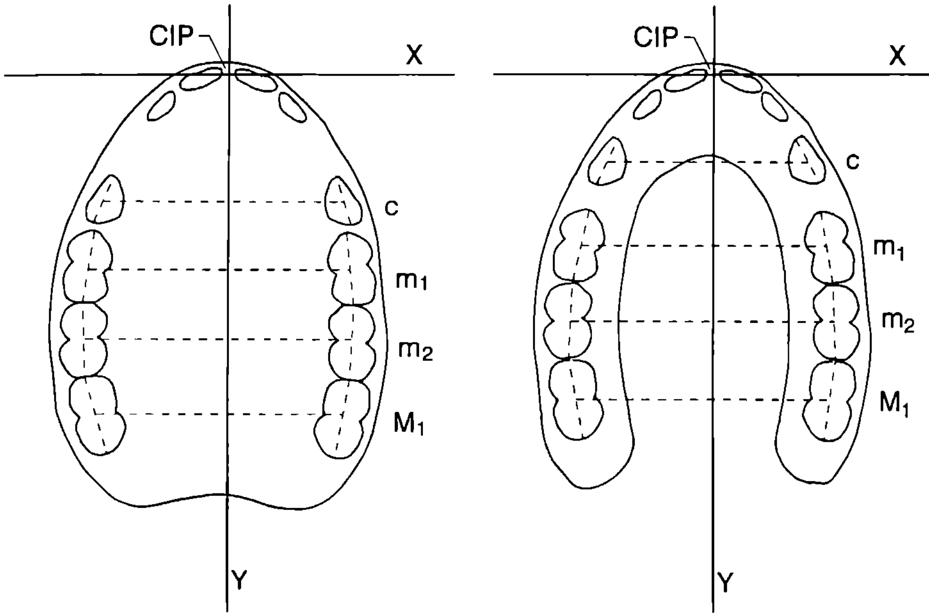


Figure 6-2: *Schematic drawing of the upper and lower jaw and their dental arches after emergence of the first permanent molars, showing the coordinate system and the measuring points.*

The antero-posterior dental arch changes were studied by calculating the increments of the distances between the central incisor point (CIP) and the lines connecting contra-lateral teeth parallel to the X-axis in μm/week: CIP - line c-c, CIP - line m_1-m_1, and CIP - line m_2-m_2.

The differences in antero-posterior changes between the jaws were analyzed by comparing the antero-posterior increments of corresponding parameters in the mandibular and the maxillary dental arch.

The vertical development in the anterior region was scored, using a 5-point scale:

1 = severe open bite, vertical distance between mandibular and maxillary incisors $\geq$ 2 mm

2 = mild open bite, vertical distance between mandibular and maxillary

incisors > 0 and < 2 mm

3 = end-to-end bite, mandibular and maxillary incisors in vertical contact

4 = mild overbite, vertical overlap between mandibular and maxillary incisors > 0 and < 2 mm

5 = severe overbite, vertical overlap between mandibular and maxillary incisors ≥ 2 mm

Scoring was performed at casts taken at 31, 103, and 153 weeks of age by one observer (J.M.O.). As the results were rather surprising, it was decided to perform an additional cross-sectional survey in an existing colony of *M. fascicularis* monkeys. This colony comprised 27 animals from 3 months to nearly 4 years of age. The anterior vertical relation in each individual was determined intra-orally using the same 5-point scale as described above by one observer (J.M.O.).

Histological procedures

In two animals of the control group and two animals of the experimental group, four fluorescent vital stains: 90 mg/kg Xylenol orange (Fluka Chemie A.G., Buchs, Switzerland), 7 mg/kg Calcein (Fluka Chemie A.G.), 30 mg/kg Alizarine (Fluka Chemie A.G.) and 30 mg/kg Tetracycline (Gist Brocades, Delft, The Netherlands) were used. Sequences of these dyes were intravenously administered every nine weeks under general anaesthesia, resulting in a polychrome sequential labelling.

The animals were sacrificed two weeks after the last labelling was performed at 152 weeks of age. They were anaesthetized, as described previously, and subsequently 0.5 mg/kg Heparin (Thromboliquine^{R}, Organon Teknika, Boxtel, The Netherlands) was administered intravenously, followed by a lethal dose of Thalamonal after some minutes. The thorax of the animals was opened and the vascular system was perfused via the arch of the aorta with physiologic saline followed by 4% neutral formaldehyde as a fixative.

After perfusion the maxilla and the mandible were dissected out and immersed in 4% neutral formaldehyde. They were then sawed into smaller blocks. One side of each maxilla and mandible was used to obtain sagittal sections, the contralateral side to obtain transverse sections. In both animals of each group the sides were alternated. From each side of the jaws alternate blocks were decalcified in 20% formic acid and 5% sodium citrate, dehydrated and embedded in Paraplast^R (Monoject Medical Inc., Athy, Ireland). From these blocks sections of 7 μm were prepared and stained with haematoxylin and eosin. The other blocks were not decalcified, but embedded in poly-methyl-methacrylate (PMMA) and sections were cut at 15 μm and examined using fluorescence microscopy. Thus, decalcified as well as undecalcified sections were obtained from all part of the maxilla or mandible.

General tissue survey and qualitative evaluation of bone deposition and resorption were carried out on decalcified sections, semi-quantitative evaluation of the amount of tooth migration as reflected by the growth and remodelling of alveolar bone was performed at undecalcified sections. Distances between the dye marker lines were estimated using an ocular micrometer and a conversion factor to obtain real distances The mean of the distances in μm between the dye marker lines was calculated for different sides of the teeth in the vertical and mesio-distal direction.

Incisors and canines were not included in this part of the study, as transition of these teeth complicated the situation in such a way that no relevant observations could be made.

Statistical procedures

Statistical analysis was only performed for the measurements on the dental casts For dental arch width measurements, the experimental period was divided in two periods: the first period from 31 to 76 weeks of age, before the first permanent molar could be used in the measurements, and the second period from 87 to 153 weeks of age in which the first permanent molars were included. Data collected in the intervening period could not be used due to a large variation in timing of the first permanent molar emergence. For the dental arch depth measurements the period from 31 to 102 weeks of age was analyzed. Thereafter, transition of the incisors took place and calculation of dental arch depth was no longer possible.

To compensate for size differences among the animals an analysis of co-variance was performed. For calibration of the transverse measurements the mean of the distances between the centres of the maxillary and mandibular first deciduous molars of each monkey at 31 weeks of age was used For calibration of the depth measurements the mean of the distances at 31 weeks of age between the central incisor point and the maxillary and mandibular first deciduous inter-molar line was used.

The paired t-test was used to analyze differences between the two periods within each group. Student's t-test was used to analyze differences between the control and the experimental group.

6.4 Results

Error of the method

The total error of the measurements on the dental casts was for antero-posterior distances about 40 μm, for transverse distances it was about 100 μm. These values were considered to be acceptable.

Transverse dental arch changes (Table 6-1)

The mean growth rates did not differ significantly between the two periods, except for the maxillary first deciduous molar width in the control group, which increased slower in the second period than in the first one.

The mean rate of the increase of any distance for any period was higher in the experimental than in the control group. However, the only significant difference was the increase in the maxillary second deciduous molar width over the total period, which was higher in the experimental than in the control animals. In the mandible no significant differences were found between the periods, or between the groups.

Histological sections of control animals showed that bone was resorbed at the cervico-palatal area of the maxillary first permanent molars (Fig. 6-2) and bone apposition took place at the apico-palatinal area indicating palatal tilting of the teeth. Bone deposition in the experimental animals was found at the cervico-palatal (Fig. 6-4) as well as at the apico-palatal area of the maxillary first permanent molar, suggesting buccal drift. In both the experimental and the control animals, bone apposition was found at the lingual side and bone resorption at the buccal side of the mandibular teeth.

Table 6-1: *Mean increments in μm/week ± SD over the first, second, and total period of the transverse distances between corresponding teeth Differences between periods (\$) = 0 05 ≤ p < 0 1, \$ = p < 0 05 Differences between groups * = p < 0 05*

Maxillary arch width

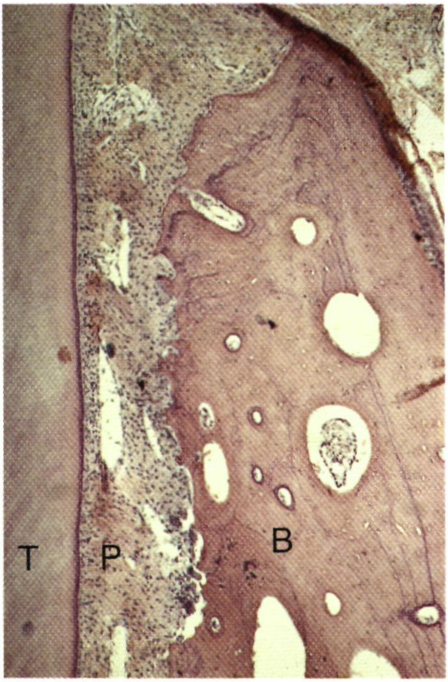
Age in weeks	Control: dec canines		first dec molars		sec dec molars		first perm molars		Experimental: dec canines		first dec molars		sec dec molars		first perm molars	
	m	SD	m	SD	m	SD	m	SD	m	SD	m	SD	m	SD	m	SD
31 - 76	45	19	46	$15^{\$}$	23	17	-	-	50	$6^{(\$)}$	46	11	24	18	-	-
87 153	37	11	25	$12^{\$}$	30	10	13	6	38	$12^{(\$)}$	36	14	42	18	19	16
31 153	39	10	33	10	29	7^{*}	-	-	42	8	41	5	40	7^{*}	-	-

Mandibular arch width

Age in weeks	Control: dec canines		first dec molars		sec dec molars		first perm molars		Experimental: dec canines		first dec molars		sec dec molars		first perm molars	
	m	SD	m	SD	m	SD	m	SD	m	SD	m	SD	m	SD	m	SD
31 76	27	20	32	14	30	22		-	42	21	37	16	38	12	-	-
87 - 153	41	10	27	9	25	11	22	11	44	14	30	17	30	18	26	17
31 153	35	10	27	10	25	11	-		41	13	34	13	34	10	-	-

Transverse inter-arch differences (Table 6-2)

The mean differences in the rate of widening of upper and lower dental arches were analyzed in both groups Comparison of the two age periods revealed significant changes in the control group. The inter-canine width and



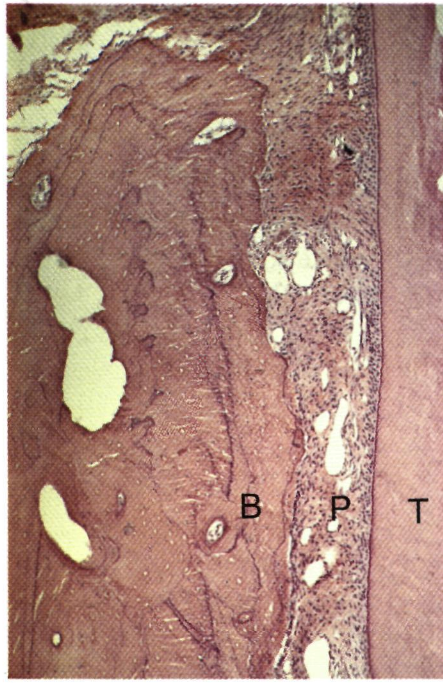


Figure 6-3: *Low power photomicrograph of a transverse paraffine section of the cervico-palatal region of the maxillary first permanent molar of the control animal showing osteoclastic resorption in the cervico-palatal region.*
H and E staining, x 25.
B = alveolar bone; P = periodontal ligament; T = tooth.

Figure 6-4: *Low power photomicrograph of a transverse paraffine section of the cervico-palatal region of the maxillary first permanent molar of the experimental animal showing resting osteoblasts.*
H and E staining, x 25.
B = alveolar bone; P = periodontal ligament; T = tooth.

the first deciduous inter-molar width in the control group increased faster in the maxilla than in the mandible in the first period In the second period this difference was significantly reduced

Comparing the findings of the control and the experimental group for the whole period no significant differences were found However, if the analysis of co-variance was involved, to compensate for initial size differences, the difference between the growth rates of the maxillary and the mandibular inter-canine width was significantly larger in the control than in the experimental group, indicating that the maxillary expansion in the experimental group in the canine region is slower than in the control group

Table 6-2: *Mean differences in increments of the maxillary and mandibular increments of the transverse distances in µm/week ± SD over the first second and total period Positive values indicate an excess of maxillary transverse growth over the mandibular one negative values the reverse*
Differences between periods $ = p < 0 05

Differences in transverse increments

	Control								Experimental							
Age in weeks	dec canines		first dec molars		sec dec molars		first perm molars		dec canines		first dec molars		sec dec molars		first perm molars	
	m	SD	m	SD	m	SD	m	SD	m	SD	m	SD	m	SD	m	SD
31 76	20	22$	15	12$	9	18			6	23	10	20	14	27	-	-
87 153	-5	11$	-2	8$	7	9	8	14	-6	10	4	10	13	17	-6	21
31 - 153	5	8	6	7	3	9	-	-	0	9	7	7	5	9	-	-

Antero-posterior dental arch changes (Table 6-3 and 6-4)

Elimination of interdigitation did not result in any significant change in the rate of increase in depth of both dental arches The increase in dental arch depth was larger in the maxilla than in the mandible This difference in the

Table 6-3: *Mean increments in µm/week ± SD over the period from 31 to 102 weeks of age of the antero-posterior distances between the central incisor point and the respective teeth.*
No significant differences between groups were found.

Antero-posterior distances

	Control								Experimental							
	dec. canines		first dec. molars		sec. dec. molars		first perm. molars		dec. canines		first dec. molars		sec. dec. molars		first perm molars	
	m	SD	m	SD	m	SD	m	SD	m	SD	m	SD	m	SD	m	SD
max.	26	16	27	18	24	20	-	-	35	8	35	7	35	7	-	-
mand.	10	9	16	11	15	13	-	-	8	5	16	5	16	4	-	-

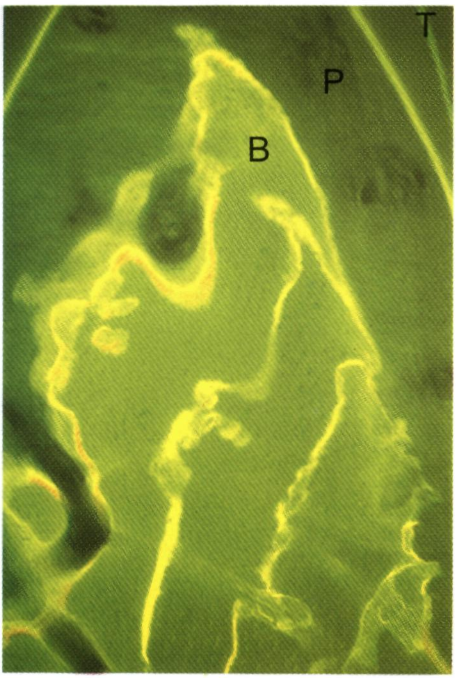
Table 6-4: *Mean differences in increments of the maxillary and mandibular antero-posterior distances in µm/week ± SD over the period from 31 to 102 weeks of age. Positive values indicate an excess of maxillary antero-posterior growth over the mandibular one; negative values the reverse.*
*Differences between groups: (*) = $0.05 \leq p < 0.1$; * = $0.01 \leq p < 0.05$.*

Differences in antero-posterior increments

	Control								Experimental							
Age in weeks	dec. canines		first dec. molars		sec. dec. molars		first perm. molars		dec. canines		first dec. molars		sec. dec. molars		first perm molars	
	m	SD	m	SD	m	SD	m	SD	m	SD	m	SD	m	SD	m	SD
31 - 102	14	8*	11	11	9	11(*)	-	-	26	8*	19	6	20	7(*)	-	-

experimental group was significantly larger in the canine region and nearly significantly larger in the region of the second deciduous molar.

Histological evaluation showed in both control and experimental animals, a distinct mesial drift at the end of the experimental period. Despite regular labelling, only the last two dye markers could be evaluated for all sites,



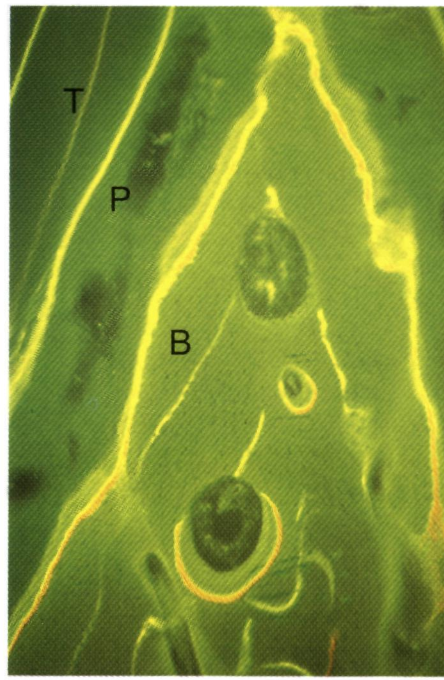


Figure 6-5: *Low power photomicrograph of a sagittal undecalcified section, of the interradicular septum of the maxillary first permanent molar of the control animal.*
x 20.
B = alveolar bone; P = periodontal ligament; T = tooth.

Figure 6-6: *Low power photomicrograph of a sagittal undecalcified section, of the interradicular septum of the maxillary first permanent molar of the experimental animal.*
x 20.
B = alveolar bone; P = periodontal ligament; T = tooth.

since most previous labels were lost due to remodelling of the alveolar bone or to bone resorption around the deciduous molars caused by erupting premolars. However, gradual differences were found in the undecalcified sections. Mesial drift of any control tooth was larger than that of the corresponding experimental one (Figs. 6-5, 6-6), and the difference between the control and the experimental animals in mesial tooth movement tended to be larger for the maxillary than for the mandibular teeth (Fig. 6-7).

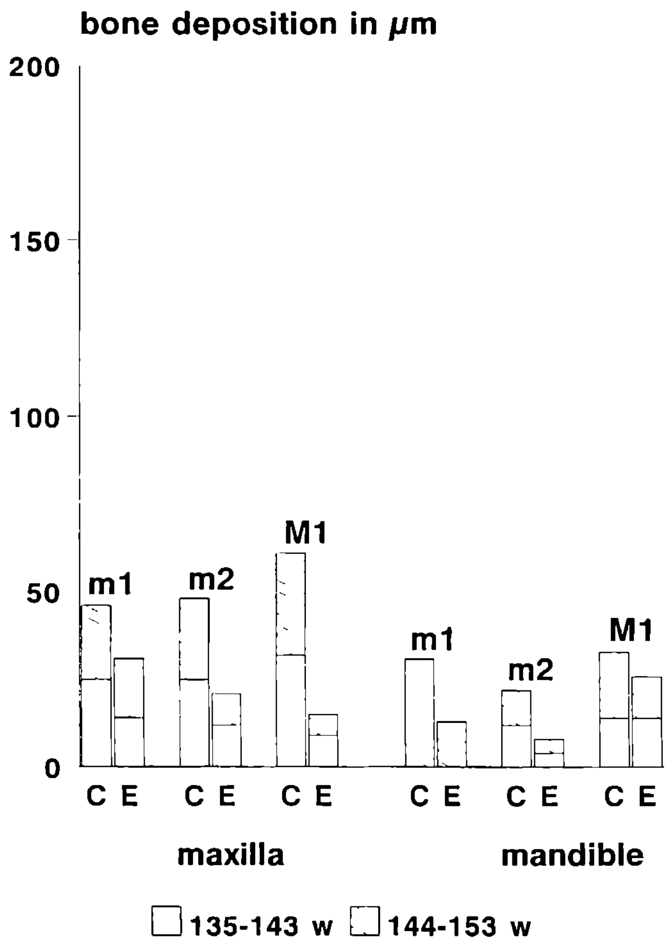


Figure 6-7: *Mean distance in µm between the marker lines for the last two periods, indicating mesial drift of the teeth involved.*

Anterior vertical changes (Figs. 6-8, 6-9, 6-10)

At the start of the experiment all animals showed an anterior end-to-end bite. At the age of 103 weeks in the control group, three out of seven animals had developed a mild or severe open bite. At 153 weeks these three animals showed a severe open bite, two others a mild open bite and only one animal showed an end-to-end relation (Fig. 6-8).

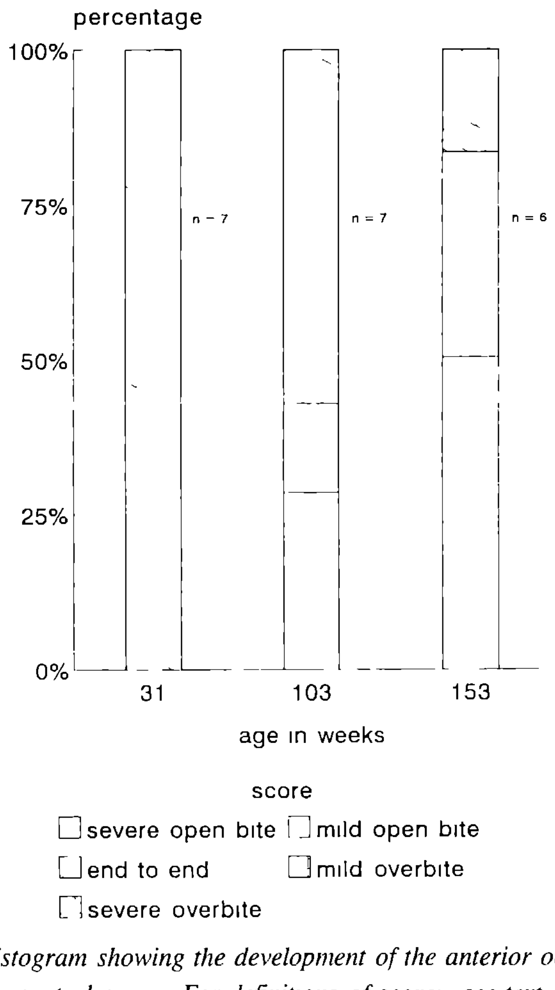


Figure 6-8: *Histogram showing the development of the anterior occlusal relation in the control group. For definitions of scores, see text.*

The development in the anterior region was different in the experimental group. At the end of the experimental period only one out of seven animals showed a severe open bite, five still showed an end-to-end relation and one animal even showed a slight overbite (Fig. 6-9).

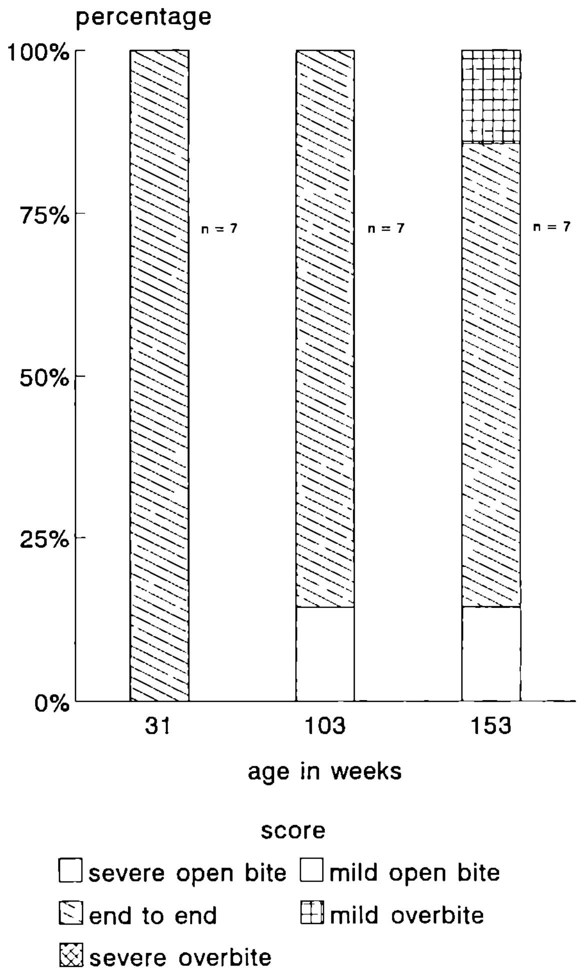


Figure 6-9: *Histogram showing the development of the anterior occlusal relation in the experimental group. For definitions of scores, see text.*

The additional survey of an existing colony of normal *M. fascicularis* monkeys showed that in these animals a tendency to the development of an open bite also existed. The percentage of animals with an open bite increased at least until the age of over three years (Fig. 6-10).

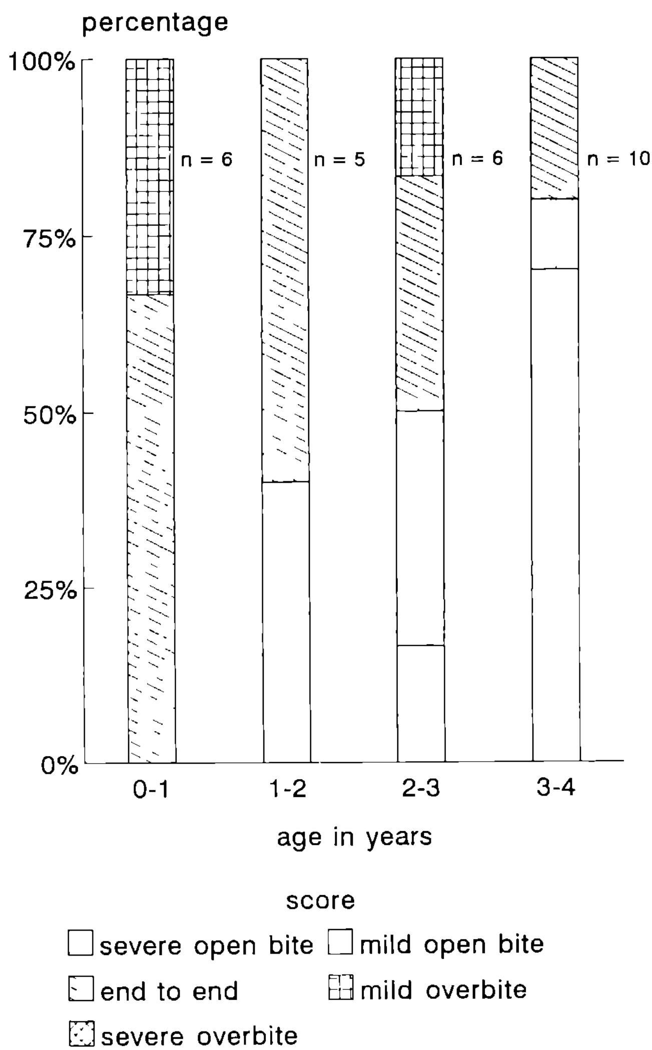


Figure 6-10: *Histogram showing the development of the anterior occlusal relation in the additional colony of normal M. fascicularis. For definitions of scores, see text.*

Posterior vertical changes

Posterior vertical tooth movements were best observed in undecalcified sections. It appeared that all those teeth moved in an occlusal direction, although at different rates. The vertical movements of the posterior control teeth seemed to be somewhat faster than the corresponding experimental ones in the period encompassing the histological evaluation. The total amount of vertical migration was about the same for all teeth histologically observed in a jaw except for the mandibular permanent first molar which, especially in the control animals, moved faster than the others (Figs. 6-5, 6-6, 6-11).

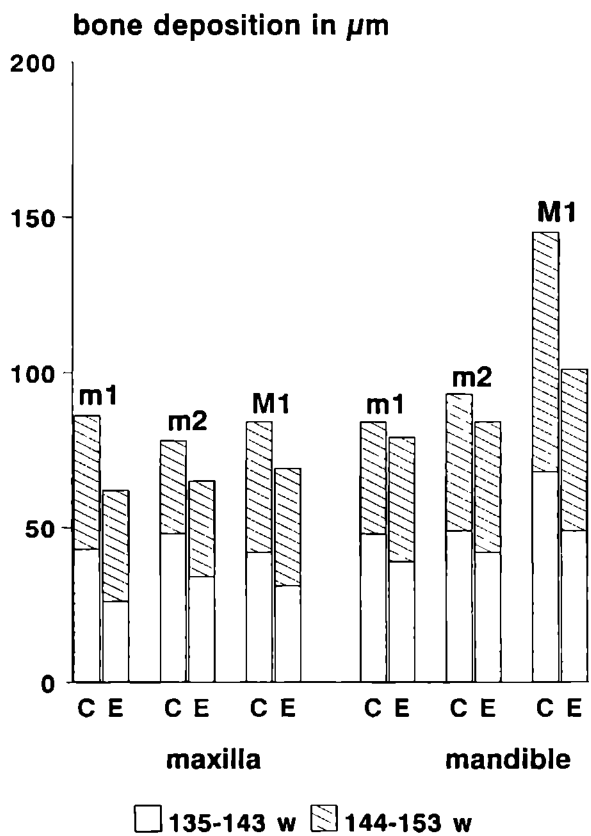


Figure 6-11: *Histogram showing the mean distances between the marker lines in μm in vertical direction indicating alveolar bone deposition.*

6.5 Discussion

The role of the interdigitation in the coordination of the development of the dentition was studied in growing *Macaca fascicularis* monkeys. These animals are considered to be a good experimental model, as their occlusal morphology and development is comparable to that in man (Van der Linden, 1971; Moffett, 1973; Watts, 1985; Sirianni, 1985; Enlow, 1990) in spite of apparent limitations and differences (Moore and Lavelle, 1974; Smith and Minium, 1983).

Interdigitation was eliminated in the experimental animals by gradually grinding the cusps, while in the control animals the dentition was left undisturbed. The effect of this intervention on the development of the dentition was studied by measurements on a series of dental casts and histological evaluation.

The transverse development is more or less constant throughout the whole experimental period as only one significant difference was found between the two sub-periods for any transverse parameter in both groups.

The transverse development of the dentition was only slightly affected in the experimental group. The only significant difference was found for the increase in distance between the maxillary second deciduous molars which was faster in the experimental animals than in the controls if the whole experimental period was considered. Although the mean increase in all other transverse distances was also faster in the experimental than in the control group, none of these differences was significant.

The histological findings showed that the maxillary permanent molars in the control group underwent a palatal tilting, which indicates a restraining effect by the mandibular dentition, which was in contrast to the findings in the experimental group. The absence of palatal tilting under experimental conditions indicated a tendency to an increased widening of the upper dental arch in the absence of interdigitation as confirmed by the dental cast measurements. According to Björk and Skieller (1976) a relative palatal movement also occurs in humans and they assumed that in the human situation this was due to the fact that the posterior segments of the dento-alveolar arch undergo a mesial migration which is directed inwards over a mesially narrowing jaw base. In *M. fascicularis*, however, no such mesially narrowing jaw base exists in the posterior region (Fig. 6-2) and therefore the results suggest that in these animals the relative palatal movement is merely due to interdigitation.

The larger buccal movement of the maxillary permanent molars under experimental conditions indicates a passive movement with the growing alveolar bone of which the growth rate is unaffected by the experimental intervention (Ostyn *et al.*, 1995b). The passive movement in the absence of interdigitation indicates a restraining effect of the mandibular dentition in the control group (Ostyn *et al.*, 1995b, 1995c). No such findings, however, were encountered for the deciduous molars in the maxilla, probably due to wearing of the occlusal surface of the deciduous molars, which mimicked the experimental interference.

In contrast to the situation in *M. fascicularis*, in humans, lack of vertical contact in the lateral segments is usually associated with a narrow maxillary dental arch. This can be explained by differences in the transverse proportions of the jaws in *M. fascicularis* and humans. In *M. fascicularis* the maxillary base is wider than the mandibular one, while in humans the opposite is true. Assuming that the mandibular dentition acts as a mould for the development of the maxillary one (Van der Linden, 1986) this means that in *M. fascicularis* the posterior mandibular dentition has a restraining effect on the widening of the maxillary dental arch, while in humans the widening of the maxillary dental arch is favoured by the mandibular dentition. This phenomenon is also illustrated by the lingual inclination of the posterior teeth in the maxilla and the buccal inclination in the mandible as found in *M. fascicularis* and the reverse inclinations in humans (Fig. 6-12).

Another situation seems to exist in the region of the deciduous canines and the first deciduous molars. The differences between the transverse growth rate of the maxilla and the mandible underwent a significant change from the first to the second period in the control group. In the experimental group, this was not the case and the rate of increase in inter-canine and first deciduous inter-molar widths was similar for the maxilla and the mandible in both sub-periods. These findings suggest that grinding of the cusps results in a relatively smaller maxillary c-c distance in the experimental than in the

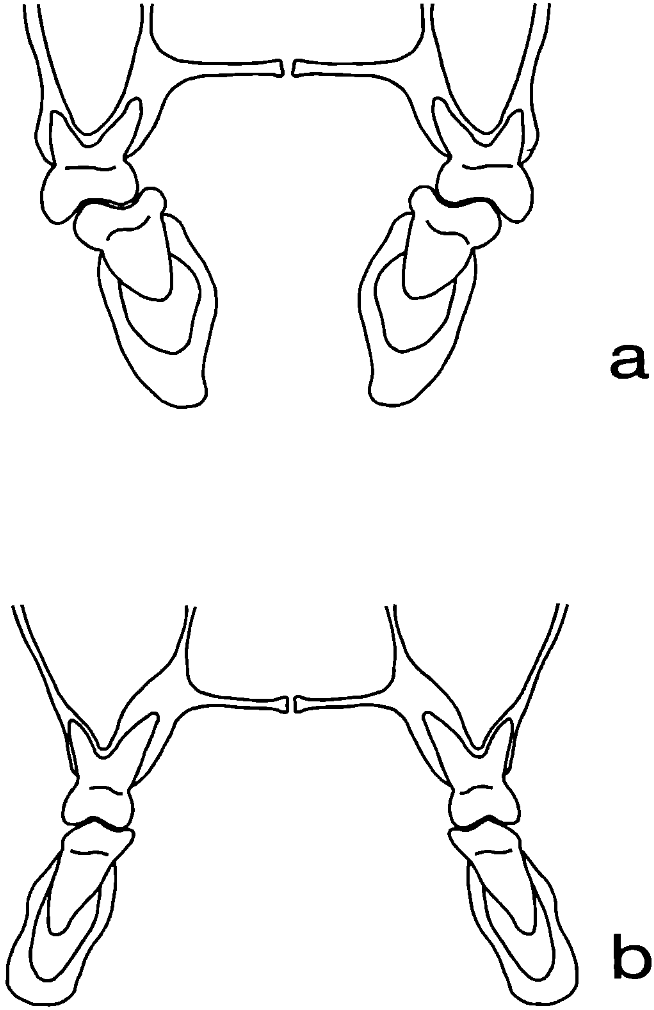


Figure 6-12: *Schematic drawings of a frontal cross-section of the dento-maxillary complex. a: Macaca species; b: man.*

control group. This means that the maxillary canines in the control group possibly are pushed in a lateral direction by their erupting mandibular antagonists.

Measurements on dental casts revealed that the increase in maxillary dental arch depth tended to be faster in the experimental that in the control group, while for the mandibular dental arch these rates were similar in both groups.

The difference in mesialization between the control and the experimental animals also tended to be larger for the maxillary than for the mandibular teeth. This was in agreement with findings from a previous study (Ostyn *et al.*, 1995c) in which measurements on lateral radiographs revealed a tendency to a dental and skeletal Class III relationship after elimination of interdigitation, while this was not the case in normal animals.

Grinding of the dentition therefore had an influence on its development in the transverse and in the antero-posterior direction. This contradicts the findings of Kantomaa and Rönning (1985) but supports the ideas of Petrovic and co-workers (Petrovic *et al.*, 1975; Stutzmann and Petrovic, 1976; Petrovic and Stutzmann, 1977). As the elimination of the interdigitation apparently does not influence any of the mandibular parameters, it is likely that the mandibular dentition develops independent of interdigitation and that it usually acts as a mould or rail for the adaptive maxillary dentition. This finding is in favour of the rail mechanism concept of Van der Linden (1986) and contradicts the hypothesis of Zingeser (1973) on this point.

An anterior open bite developed during the experimental period in all animals of the control group except one. Elimination of interdigitation in the experimental group seemingly impeded the development of an anterior open bite. The development of an anterior open bite during growth seems to be a normal feature in *M. fascicularis* as was confirmed by additional observations in a sample of 27 normal *M. fascicularis* from six months to over three years of age. As the dental development in the control and the experimental group agreed, the absence of this phenomenon in the experimental group probably is related to the fact that the normal vertical displacement of the maxillary structures in the experimental group was affected (Ostyn *et al.*, 1995c) resulting in a more pronounced counter-clockwise rotation of the mandible and a more end-to-end relationship in the anterior region.

It can be concluded that elimination of interdigitation leads to changes in the development of the maxillary dental arch. The mandibular dental arch seems to develop independent of any occlusal interference and might play a guiding role in the normal development of the maxillary dental arch by means of interdigitation. This is in accordance with the rail mechanism as suggested by Van der Linden (1986).

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Chapter 7

General discussion

The purpose of this study was to investigate the contribution of interdigitation of the dentition to the growth of the maxillo-facial complex. An experimental set-up was chosen in which the growth centres were left undisturbed and only the interdigitation was eliminated. *Macaca fascicularis* monkeys were chosen as experimental model as the growth of the maxillo-facial complex of *Macaca species* appears to be highly comparable to that in man (Duterloo and Enlow, 1970; Van der Linden, 1977; Moffett, 1973; Sirianni, 1985; Watts, 1985; Enlow, 1990) and therefore these animals yield important advantages over other non-human primates and non-primates in spite of apparent limitations and differences (Moore and Lavelle, 1974; Smith and Minium, 1983). Furthermore, *Macaca species* is particularly suited to study the relation between craniofacial growth and occlusion, as their occlusal relations, as in man, are maintained in a changing maxillo-mandibular relationship after establishment of a solid interdigitation (Baume and Becks, 1950 Elgoyhen *et al.*, 1972; Swindler and Sirianni, 1973; McNamara *et al.*, 1976; Nanda *et al.*, 1987).

Two groups of animals were longitudinally followed during their growth from 30-153 weeks of age. The animals in the control group were left undisturbed, except for the placement of bone and tooth markers as measuring points. The cusps of the maxillary and mandibulary deciduous and permanent molars in the experimental group were ground gradually as soon as possible after emergence, without disturbing their vitality. These animals were also provided with bone and tooth markers. In both groups skeletal growth was left undisturbed.

Growth of the maxillo-facial complex was studied in both groups, using a series of standardized lateral and occlusal radiographs, and series of dental casts of both jaws. A limited number of animals was studied histologically using normal histological and vital staining techniques.

Data derived from measurements on these records can be divided into two categories, one concerning the skeletal changes, and the other concerning changes in the dentition. Both categories are measured using metallic implants and, as the placement was not completely uniform, increments instead of real distances have been used to describe growth and displacement. Plots revealed that the total observation period could be devided into subperiods in which growth and displacement took place at a constant rate. Statistical analysis was performed using the mean rates per subperiod, expressed as μm/week.

It appears that elimination of interdigitation induces structural and positional changes in the growing maxillo-facial complex. The most affected area appears to be the maxilla and particularly its vertical relationship to the cranial base. The maxilla moves less "downward" in the experimental than in the control group, but compensation for this phenomenon is found in an increase in the vertical growth of the alveolar processes of both jaws. The decrease in downward displacement can be explained by a combination of factors. Elimination of interdigitation allows the mandible to occlude in a more anterior position than normally is the case. This results in a more anterior point of masticatory force application on the maxillary structures. The change in mechanical circumstances could easily provoke a restraint in the normal downward displacement of the maxilla as the maxillary structures of the non-human primate at young age are highly adaptable (McNamara, 1977; Altuna and Woodside, 1985; Woods and Nanda, 1988).

No significant differences in transverse maxillary growth were found between the experimental and the control group, indicating that neither mid-palatal sutural growth nor the transverse mutual rotation of both maxillary halves as described by Björk and Skieller (1976) seems to be under control of interdigitation. The same holds true for the forward displacement of the maxilla.

The size of the mandible was not measurably influenced by the experiment although it attained a significant more anterior position relative to the maxilla, leading to a skeletal Class III relationship. Its shape, however, was slightly affected as was demonstrated by a temporary larger increase in the gonial angle in the experimental group. It is also likely that the anterior mandibular transposition is correlated to an altered position of the condyle and it is reasonable to assume that this leads to adaptive response and remodelling in the condyle and glenoid fossa.

The changes in position and shape of the mandible by the experimental intervention clearly demonstrate that interdigitation acts as a guidance system for the development of the maxillo-mandibular relationship.

Sagittal inter-arch changes in the dentition are mainly caused by skeletal changes, they are of rather secondary nature. Elimination of interdigitation leads indirectly also to a dental Class III relationship as the mandibular molars in the experimental as well as in the control group remained stable in relation to the mandibular basal bony structure.

In contrast to this change in the sagittal plane, the maxillary dental arch width increased in certain areas after elimination of interdigitation, although the surrounding skeletal parts did not. This was revealed by comparison of measurements on dental casts and occlusal radiographs. The larger buccal drift of the maxillary permanent molars under experimental conditions was limited and had to be attributed to the fact that the elimination of interdigitation allowed a less palatal inclination of the buccal crowns. The restraining effect by the mandibular dentition in the control group, caused a palatal tilting of the molar crowns. A relative palatal movement of the permanent molars occurs also in humans according to Björk and Skieller (1976), but in that case it is due to the fact that the posterior segments of the dento-alveolar arch undergo a mesial migration which is directed inwards over a jaw base which becomes narrower in the mesial direction. Such a narrowing jaw base does not exist in *M. fascicularis* monkeys and thus the relative palatal movement is solely due to interdigitation.

Differences in transverse dental arch widening between both groups were only found for the maxillary second deciduous molar. The fact that first deciduous molars did not show such differences is probably due to their more extensive wearing resulting in a less pronounced interdigitation, and thus in a decreased influence of the experimental intervention.

During the experimental period an anterior open bite developed in all animals of the control group except for one. Elimination of interdigitation seemingly impeded the development of an anterior open bite. The fact that the presence of an anterior open bite is a normal feature in growing *M. fascicularis* was confirmed by additional observations in a sample of 27 normal *M. fascicularis* monkeys from 26 to 162 weeks of age (Ostyn *et al.*, 1995a). The absence of this phenomenon in the experimental group might be related to the fact that the normal vertical displacement of maxillary structures was affected in the experimental group (Ostyn *et al.*, 1995b) causing a more pronounced counter-clock-wise rotation of the mandible and by that a more end-to-end relation in the anterior region

The effect of interdigitation is in humans sometimes eliminated by tongue interposition between the occlusal surfaces in the posterior region This usually gives rise to a narrow maxillary arch which seems to be in contrast to the findings in *M fascicularis*, where absence of interdigitation resulted in a broader maxillary arch This discrepancy should not be considered as a falsification of the rail mechanism hypothesis but it is probably related to anatomical differences between humans and non-human primates In humans the growing mandible is wider than the maxilla and according to the rail mechanism hypothesis the mandibular dentition forces the maxillary dentition in a buccal direction This is also suggested by the buccal crown inclination of maxillary premolars and molars and the lingual crown inclination of premolars and molars in the mandible Elimination of interdigitation therefore will lead to a relatively narrow maxillary dental arch

In non-human primates the reverse is true The growing mandible is narrower than the maxilla As a consequence the rail mechanism acts as a restraining factor for the widening of the maxillary dental arch This also reflected in the crown inclination in the buccal area The maxillary premolar and molar crowns are palatally inclined, whereas the crown inclination of the mandibular premolars and molars is in a buccal direction Therefore elimination of interdigitation in non-human primates will result in a widening of the maxillary dental arch

So, in summary, the grinding of the dentition in *M fascicularis* has an influence on its development in the antero-posterior and the vertical direction This contradicts the findings of Kantomaa and Ronning (1985) and supports the ideas of Petrovic and co-workers (Petrovic *et al* , 1975, Stutzmann and Petrovic, 1976, Petrovic and Stutzmann, 1977) Elimination of the interdigitation apparently does not influence any of the mandibular parameters, and thus it is likely that the mandibular dentition develops independent of interdigitation and that it might act as a mould or rail for an adaptive maxillary dentition This finding is in favour of the rail mechanism concept of Van der Linden (1986) and contradicts the hypothesis of Zingeser (1973) who stated that the maxilla serves as a template to which mandibular growth adapts

From the above findings it also can be concluded that the interdigitation is an important factor in the control of the antero-posterior relationship between the jaws and their dentitions. This view emerged also from the study of Elgoyhen *et al.* (1972) in normal *M. mulatta.* They observed differences between mandibular and maxillary growth in sagittal direction, while the occlusion remained relatively constant. They suggested that the steeply inclined cuspal planes were a contributing factor to the occlusal homeostasis.

Neither the maxillary, nor the mandibular bone is affected in its sagittal and transversal growth by the experimental intervention which means that the effect of functional transmission of forces between the jaws, as supposed by the rail mechanism of Van der Linden (1986) and in accordance with the study by Joho (1973), is restricted to the dentition.

Our findings fit also in the concept of Sarnat (1958, 1976) that the interdigitation plays a guidance role in the maxillary dental arch growth and they confirm the opinion of Nanda *et al.* (1983a, 1983b) that the coordinated reduction in growth of both dental arches as was found after Le Fort I osteotomies in *M. fascicularis,* was tuned through interdigitation.

A contribution of interdigitation on the coordination of the development of the dentition in both jaws is also assumed in the anthropological and clinical studies from Slagsvold (1971), Fishman (1976), and Helm and Prydsö (1979). Brace (1977) even stated that the cusp form in the human dentition is not related to the ability of effective mastication and that the main importance of interdigitation is its action as a guiding system for the developing face and dentition. Also Petrovic *et al.* (1976, 1977) in their hypothetical servo-system stress the importance of a cybernetic peripheral comparator for the coordination of the growth of the upper and lower jaw, and for the maintenance of an optimal occlusal relation.

When extrapolated to the human situation it seems therefore reasonable to accept that interdigitation is probably most responsible for guiding the teeth into their proper occlusal relation with the opposing arch, a mechanism which is also known as the cone-funnel mechanism (Van der Linden, 1983). Once a good interdigitation is realized, each closing movement of the jaws will end in the same relationship between the two dental arches. A well established interdigitation of the posterior teeth will thus be maintained during growth and in that situation soft tissues are unable to change occlusion.

Since transversal bone growth of the maxilla appears not to be under control of interdigitation, lack of normal vertical contact in the posterior region interferes with the transverse development of the maxillary dental arch and allows more freedom for functional factors and intrinsic growth of the surrounding maxillary structures to exert effect on maxillary dental arch width. Also in consequence, the cone-funnel mechanism cannot operate, nor the rail mechanism; the normal occlusal homeostasis will be disturbed and the final outcome then will be a deviation of the normal occlusal pattern.

A deviating transversal occlusion which, associated with posterior open bites is probably not caused by altered palatal sutural growth but merely by a lack of attuning both dental arches.

This study emphasizes that interdigitation contributes to the coordination of the development of the oro-facial structures. It therefore should be considered in orthodontic diagnosis and treatment (Van der Linden, 1991).

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Chapter 8

Summary

The aim of the present investigation was to study the role of interdigitation in the coordination of the maxillary and mandibular growth and the development of their dentition.

As an experimental animal, the *Macaca fascicularis* monkey was used, in which the interdigitation was eliminated by grinding of the cusps of the deciduous canines and molars and the first permanent molars. Dental and skeletal changes over time were analyzed using series of standardized occlusal and lateral radiographs, series of dental casts, and histological techniques.

Chapter 1 presents a review of the literature dealing with the coordination mechanism for maxillary and mandibular growth and the development of the dentition. It is mainly focused on the role of mechanical stimuli originating from the dentition in this mechanism. The cone-funnel mechanism is generally accepted as a major factor in the establishment of a proper occlusion. The opinions on the possible role of interdigitation in skeletal and occlusal development, however, are conflicting. The importance of interdigitation is emphasized, on a hypothetical level, by several authors, and also in clinical orthodontics a contribution of interdigitation to maxillo-facial development is often assumed. However, in experimental approaches so far, the original craniofacial development has been disturbed, which limits the extrapolation of the findings to normal growing systems. To meet this shortcoming, in the present study the contribution of interdigitation to the development of the maxillo-mandibular complex will be investigated using an experimental set-up in which growth centres are not directly affected.

The use of *M. fascicularis* in this field of research is advocated and the chapter ends with questioning the rail mechanism hypothesis as formulated by Van der Linden (1986).

Chapter 2 describes normal developmental characteristics for the dentition of juvenile *M. fascicularis* as derived from radiographs and relates them to chronological age. As tooth development is a progressive and continuous intra-osseous process which is independent from environmental factors, these data can be used to estimate the age of young *M. fascicularis* monkeys with an unknown date of birth.

Chapter 3 gives a description of the dento-facial growth and development in the juvenile *M. fascicularis* using standardized lateral cephalometric radiographs. Growth data were obtained by analyzing the changes in relation to the frontal bone implant and the Anterior Cranial Base line and also in relation to implants placed in the jaws. The results suggest that the dento-facial growth and development in the juvenile *M. fascicularis* and in humans have many points in common, and therefore *M. fascicularis* appears to be a good model for further studies in the regulation of the processes involved.

Chapter 4 deals with the role of the interdigitation in sagittal growth of the maxillo-mandibular complex using standardized lateral cephalometric radiographs. It appeared that elimination of interdigitation resulted in a deviating antero-posterior relationship between the jaws and in a significant inhibition of the vertical displacement of the maxilla in the second half of the experimental period, while the total facial height was not noticeably affected. A more prognathic skeletal relationship and a more mesial occlusion developed as a result. It can be concluded that interdigitation plays a role in the regulation of vertical and antero-posterior growth and development of the maxillo-mandibular complex in *M. fascicularis* monkeys.

In **Chapter 5** standardized occlusal radiographs are studied in order to evaluate the role of interdigitation on transverse maxillary growth and dental arch development. Midpalatal sutural growth appeared to be independent of interdigitation. The maxillary dental arch, however, showed locally a greater increase in width under experimental conditions. The maxillary dental arch can be considered to be guided by that of the mandible through interdigitation of the posterior teeth.

Chapter 6 deals with the study of the development of the dentition on a series of dental casts and at the histological level by the use of vital staining techniques. The finding that the maxillary dental arch broadened faster in the experimental group was confirmed by this part of the study. The results seemed to be contradictory to the situation in humans, where lack of interdigitation in most cases leads to a narrowing of the maxillary dental arch. However, differences in the proportional relationship between both jaws in humans and *M. fascicularis* can explain this discrepancy. The mechanism itself is the same in both species, but the direction of its action, and therefore the outcome of the mechanism is the reverse.

As the mandibular dental arch development appeared to be not affected by the experimental interference, it could be considered to be independent of interdigitation. Experimental intervention also led to less prevalence of anterior open bites, which is a normal feature in the developing *M. fascicularis*.

Chapter 7 analyzes earlier findings and extrapolates them to the human situation leading to theoretical reflections on clinical orthodontics.

The **Appendix** describes the mathematical analysis used to detect possible unequal transverse development of both maxillary halves, which could dissimulate eventually experimentally induced differences. This analysis revealed that asymmetries occurred at random, and therefore it was concluded that they did not interfere with the results.

Chapter 9

Samenvatting

Het doel van het onderhavige onderzoek was het verkrijgen van een beter inzicht in de mogelijke coördinerende rol die interdigitatie zou kunnen spelen bij de groei van de maxilla en de mandibula en bij de ontwikkeling van hun dentitie.

De Java aap (*Macaca fascicularis*) werd gebruikt als experimenteel model. In deze dieren werd de interdigitatie geëlimineerd door het beslijpen van de knobbeltoppen van de melkhoektanden, de melkmolaren en de eerste blijvende molaren. Dentale en skeletale veranderingen in de tijd werden geanalyseerd met behulp van series gestandaardiseerde laterale en occlusale röntgenopnames, series gebitsmodellen en histologische technieken.

In **Hoofdstuk 1** wordt een literatuuroverzicht gegeven met betrekking tot het coördinatie-mechanisme dat de afstemming van de maxillaire en mandibulaire groei bepaalt en de rol die dit mechanisme speelt in de ontwikkeling van de dentitie. De rol van mechanische stimuli afkomstig van de dentitie staat hierbij centraal. Het wordt algemeen aanvaard dat het kegel-trechter mechanisme een hoofdrol speelt bij het instellen van een juiste occlusie. De meningen over de mogelijke rol die de interdigitatie zou kunnen spelen bij de verdere ontwikkeling van de occlusie en de skeletale delen zijn echter tegenstrijdig. Op hypothetisch niveau wordt het belang van de interdigitatie bij deze processen benadrukt door verschillende auteurs en ook in de klinische orthodontie wordt een bijdrage van de interdigitatie aan de maxillo-faciale ontwikkeling vaak verondersteld.

De benadering van deze problematiek tot nu toe heeft steeds geleid tot onderzoek waarbij de cranio-faciale ontwikkeling experimenteel werd verstoord, waardoor de extrapolatie naar normaal-groeiende individuen wordt bemoeilijkt. Om aan deze tekortkoming tegemoet te komen worden in het onderhavige onderzoek de groeicentra ongestoord gelaten. Deze benadering maakt een nader onderzoek van het railmechanisme zoals gepostuleerd door Van der Linden (1986) mogelijk.

In **Hoofdstuk 2** wordt op basis van series gestandaardiseerde röntgen opnames de relatie beschreven tussen de ontwikkelingsstadia van de dentitie in de juveniele *M. fascicularis* en zijn chronologische leeftijd. Aangezien tandontwikkeling een continu voortgaand proces is dat zich in het kaakbot afspeelt en dat niet afhankelijk is van omgevingsfactoren kunnen deze gegevens gebruikt worden om van dieren met een onbekende geboortedatum de leeftijd te schatten.

In **Hoofdstuk 3** wordt een beschrijving van de normale dento-faciale groei en ontwikkeling in de juveniele *M. fascicularis* gegeven, gebaseerd op gestandaardiseerde laterale röntgen opnames. De gegevens met betrekking tot de groei werden verkregen door de analyse van de veranderingen in de tijd gerelateerd aan metalen botmerkers in het *os frontale* en de zogenaamde Anterior Cranial Base Line. Bovendien werden de veranderingen ten opzicht van botmerkers die in de kaken waren geïmplanteerd, geanalyseerd. De resultaten geven aanwijzingen dat de dento-faciale groei en ontwikkeling in *M. fascicularis* overeenstemming vertoont met de humane situatie. *M. fascicularis* kan dan ook beschouwd worden als een goed modelsysteem.

In **Hoofdstuk 4** wordt een onderzoek beschreven naar de rol van de interdigitatie bij de sagittale groei van het maxillo-mandibulaire complex, waarbij gebruik gemaakt werd van series gestandaardiseerde laterale röntgenopnames. Het bleek dat de eliminatie van de interdigitatie resulteerde in een deviatie van de normale sagittale relatie tussen de kaken en in een significante remming van de verticale verplaatsing van de maxilla in de tweede helft van de experimentele periode. Dit resulteerde echter niet in een meetbare afwijking van de totale gelaatshoogte. Er ontwikkelde zich een meer prognate skeletale relatie en een meer mesiale occlusie onder invloed van de experimentele ingreep. Er werd geconcludeerd dat interdigitatie een rol speelt in de regulatie van de verticale en sagittale ontwikkeling van het dentofaciale gebied in *M. fascicularis*.

In **Hoofdstuk 5** wordt een onderzoek beschreven aan de hand van series gestandaardiseerd occlusale röntgen opnames met het doel meer inzicht te krijgen in de rol van de interdigitatie op de transversale groei van de maxilla en de ontwikkeling van de maxillaire tandboog. De groei van de midpalatinale sutuur bleek onafhankelijk te zijn van de interdigitatie. Lokaal, nam de breedte van de maxillaire tandboog echter sneller toe onder de experimentele omstandigheden. Er kan worden geconcludeerd dat de breedtegroei van de maxillaire tandboog wordt gestuurd door de interdigitatie met de distale elementen van de mandibula.

In **Hoofdstuk 6** wordt een onderzoek beschreven naar de ontwikkeling van de dentitie onder experimentele en controle omstandigheden. Hierbij werd gebruik gemaakt van series gebitsmodellen en histologische technieken met vitaal kleuring. Het feit dat de maxillaire tandboog onder experimentele omstandigheden sneller verbreedt, zoals beschreven in Hoofdstuk 5 werd in dit deel van het onderzoek bevestigd. Deze resultaten schijnen in tegenspraak te zijn met de humane situatie, waarbij een gebrek aan interdigitatie meestal leidt tot een smallere maxillaire tandboog. Dit verschil kan echter verklaard worden doordat de transversale verhoudingen tussen de boven- en onderkaak in de mens en in *M. fascicularis* verschillend zijn. Het mechanisme zelf is identiek in beide species, maar de richting waarin het werkt is tegengesteld.

Aangezien de ontwikkeling van de mandibulaire tandboog niet bleek te worden beïnvloed door de experimentele ingreep, kan deze als onafhankelijk van de interdigitatie worden beschouwd. De experimentele ingreep leidde bij *M. fascicularis* tot een verminderde prevalentie van open beten, die bij normale *M. fascicularis* veelvuldig voorkomen.

In **Hoofdstuk 7** worden de gegevens uit de voorafgaande hoofdstukken geïntegreerd besproken en ze worden geëxtrapoleerd naar de humane situatie, hetgeen leidt tot enige theoretische beschouwingen over klinische orthodontie.

In de **Appendix** wordt een mathematische analyse beschreven die gebruikt is om asymmetrieën tussen de beide helften van de maxilla, die eventueel tijdens de ontwikkeling zouden kunnen voorkomen, op te sporen. De analyse toonde aan dat asymmetrieën *at random* voorkomen en dat ze derhalve niet interfereren met de resultaten.

Symmetry analysis

The statistical analysis of the data on transversal growth of the dento-maxillary complex was based on the assumption that this growth was symmetrical. However, in case asymmetries would develop, they might obscure existing differences between the experimental and the control group. This stresses the importance of a further analysis of symmetry.

Tooth and bone markers were used to calculate changes in the relative transverse positions of the teeth in the maxillary bone for the left and right side respectively using the x-coordinates of the original dataset. The relative position of a tooth in the maxillary bone is than given by the difference in their x-coordinates: $| T\text{-}B |$ and the change in the relative position over a certain period is given by the equation:

$$| T_e\text{-}B_e | - | T_s\text{-}B_s | \quad (1)$$

in which T_e and B_e are the coordinates at the end of the period and T_s and B_s are those at the start.

Now, if an asymmetry develops, the outcome of equation (1) for corresponding left and right tooth and bone markers will be different. This difference, given by

$$\Big| \; \Big| \{ | T_e\text{-}B_e | - | T_s\text{-}B_s | \} \Big|_L - \Big| \{ | T_e\text{-}B_e | - | T_s\text{-}B_s | \} \Big|_R \; \Big| \quad (2)$$

is used as a symmetry index, which is zero if the development on the left and the right side is identical, and which becomes positive in case of asymmetries.

The symmetry index is calculated for the region of the deciduous first and second molar and the permanent first molar separately.

Statistical analysis was performed to answer the following questions:

1. Is the symmetry index dependent of the position of a tooth in the dental arch?
2. Is the symmetry index dependent of the age of the animals or on the length of the period over which it is measured?
3. Is the symmetry index in the experimental group different from that in the control group?

Ad 1.

The mean values of the symmetry index for the different teeth (m_1, m_2, M_1) were compared mutually with the Student's t-test. Eight separate tests were performed. Two tests resulted in significant differences with p-values of 0.03 and 0.01 respectively. However, the amount of tests compels the application of Bonferroni's correction, after which none of the differences appeared to be significant. This being the case, the variables of the different sites were pooled for further analysis.

Ad 2.

The total experimental period was divided in three subperiods from 30-80, 80-120 and 120-155 weeks of age respectively. The mean symmetry indexes of the pooled data for these subperiods were compared mutually using Student's t-test. No significant differences were found. Also comparison of the subperiods and the main period from 30-155 weeks of age revealed no significant differences.

Ad 3.

Comparison of the data for the experimental and the control group for the subperiods and the main period has been performed, using Student's t-test. No significant differences in symmetry indexes were found (Table A-1).

Table A-1: *Mean symmetry indexes (m) and SEM in 0.01 mm of the pooled data.*

Age in weeks	Control			Experimental			t-test
	n	m	SEM	n	m	SEM	
30 - 80	7	34	7	7	38	12	NS
80 - 120	6	34	7	7	40	12	NS
120 - 155	6	50	14	6	37	7	NS
30 - 155	4	53	31	7	49	10	NS

Although the measurements reveal that the development of the dental arch is not exactly symmetrical, the results of the statistical analysis give no indication pointing in a certain direction.

It can be concluded that no systematic influence of the position of a tooth in the dental arch, the age period or the experimental intervention, on the magnitude of the asymmetry can be demonstrated and that the occurring asymmetries are randomly distributed.

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Curriculum vitae

Jan Maurice Cornelius Ostyn was born on June, 30st, 1952 in Leuven (Belgium). In 1971 he completed his classic languages education at the Bishop's College in Veurne (Belgium). In 1974 he resided in Israel as a kibbutz volunteer.

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He completed his studies in orthodontics in 1985 at the Department of Orthodontics, State University of Gent (Belgium) under supervision of Professor L.R. Dermaut.

From his graduation until February, 1994 he was consultant in orthodontics at the Graduate Training Centre of the Dental School of the Catholic University of Leuven in Brugge (Belgium). In his spare time he conducted the present study at the Department of Orthodontics and Oral Biology, University of Nijmegen.

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